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YAWS AND SYPHILIS. TWO DISEASES OR ONE?*

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The discussion as to the identity or otherwise of yaws and syphilis has for long been rather of academic interest; recent developments in the treatment of yaws have, however, given a fresh and practical impulse to the subject. By modern methods it is possible to get rid of the secondary eruption of yaws easily and rapidly; now, if yaws is in fact a condition which is closely analogous to syphilis, there appear to be two eventualities to consider in regard to its treatment. Firstly an inadequate treatment, which caused the disappearance of the skin eruption while not destroying the infection in the body, might result in a neurotropic effect, so that the nervous system might become seriously involved. Secondly, an adequate but premature treatment, by which the spirochaetes throughout the body were entirely destroyed, might lead to a different, but no less important sequel. The important experiments of SELLARDS and GOODPASTURE (1923) suggest clearly the nature of the problems involved. These authors record that they treated with neosalvarsan four patients who had had yaws for three months, eight months, one year and two years, and whose Wassermann test was positive; six months later all four, now Wassermann negative, were inoculated with yaws material; the case with yaws for only three months at the time of treatment developed typical granulomata, the eight-months case showed slow growing granulomata which spontaneously regressed; the other two cases developed abortive lesions which disappeared promptly. The authors concluded that active immunity develops in yaws late in the secondary stage.

If yaws infection is capable of protecting against venereal syphilis, then by curing the yaws of children prematurely we are presumably

* Professor Blacklock questions the soundness of much of the current beliefs about yaws and its relation to syphilis. His arguments will doubtless receive open-minded attention.—Ed.

removing their immunity against subsequent syphilitic venereal infection. The prevention of yaws infection in childhood or its cure by successful treatment may thus be a serious step unless the danger of venereal infection later can be obviated. It is not that syphilis in itself, and in its sequelae as it affects the individual, is any worse than yaws, but because of the congenital infection which occurs when the spirochaetal attack is postponed to the marriageable age. Transplacental transmission, with resulting intrauterine deaths, premature stillbirths and congenital infection introduces the possibility of grave racial deterioration.

No one disputes the fact that there are striking differences between yaws in the tropics and venereal syphilis in Europe ; facility in pronouncing a case of yaws to be yaws, however, does not affect the real question at issue, which is, whether or not yaws may be a form of syphilis. With regard to this question we must finally come to some conclusion as to what basis is to be adopted for our evidence. Given that the morphological characters and staining reactions of the parasites found are identical and that in addition the serological and therapeutical tests in those affected are similar, are we entitled to say that therefore yaws and syphilis are due to the same cause ? Or can we deliberately set aside all these tests as completely valueless in favour of certain other tests which we accept as proving that yaws and syphilis are due to different causes ? If we do, then it is not unnatural that we should be asked for details as to what these certain other tests are, and that we should be expected to put forward for each one convincing proof of its reliability.

A serologist in England carrying out the Wassermann test is prone to interpret a positive reaction as evidence that the patient's serum contains syphilitic antibody. If the patient were then stated not to have syphilis but leprosy, evidence of this would be expected, *e.g.*, demonstration of *Mycobacterium leprae* or, failing that, clinical evidence of a convincing kind plus the fact, as shown by GOODPASTURE (1923), that antisyphilitic treatment administered to the leper failed to render the blood test negative ; should malaria be adduced as producing the positive blood result, evidence of the presence of malaria parasites would be required. If, however, yaws were stated to be the cause of the positive reaction what evidence could be produced in favour of this assertion ? Not the parasite, because both by dark ground examination and staining tests the serologist, finding *S. pallida*, would fail to be convinced Nor would a therapeutic test by arsenic be a likely means of differentiating this blood-positive case as yaws to his satisfaction. What then are the tests which are to convince the serologist that he was wrong in declaring this to be a syphilitic serological reaction ? The answer is in the tabular statements to be found in most text-books which deal with yaws, and one of these we may now consider.

1. *Yaws* : *not congenital. Syphilis* : *congenital.*

We may accept as admitted, by some observers, that there is a little evidence that yaws infection is transmitted to the foetus *in utero*.

Now let us look at the opposed statement, namely, that syphilis *is* congenital, and consider in how far this is true. Syphilis is not the name of a single and uniform clinical entity ; on the contrary, it presents so many forms that it is usually divided into several distinct clinical categories. We may select a main division of syphilis into two

groups, namely, (1) syphilis venereally acquired, with or without chancre, and (2) syphilis acquired non-venereally. This second group may be further subdivided into :—

(*a*) Adult syphilis, with extragenital primary sore.

(*b*) The syphilis of early childhood with extragenital, or more rarely, with genital primary sore.

(*c*) Congenital syphilis with no primary sore, either genital or extragenital.

With regard to our first main division, namely, venereally acquired syphilis, the statement that it is congenital may be admissible, but only if we qualify it by a series of reservations, to the effect that transmission to the partner in marriage does not occur inevitably in venereally acquired syphilis, that the infected mother may not transmit the disease to her child, that the lapse of even a moderate time from the date of infection of the mother may greatly diminish the chances of its being transmitted transplacentally, that it may be transmitted by her quite irregularly, not to one child but to the next, and that it may even be transmitted to one and not to the other of twins. When we endeavour to ascertain in what percentage of venereally acquired syphilis the disease will be passed transplacentally to the foetus, we obtain figures which are sometimes surprisingly low. A recent figure by ABRAHAM (1932) is 14·1 per cent. of congenital children in a series of births from ninety-two Wassermann positive women.

Our second main division, namely, syphilis acquired non-venereally, has for its first sub-division that of adult syphilis with extragenital primary sore, and for its second the syphilis of early childhood with extragenital or, more rarely, genital primary sore. For neither of these two groups have I been able to find adequate figures which are of assistance to us in trying to decide whether such forms of syphilis are commonly transmitted to the foetus.

As regards our third subdivision, namely, congenital syphilis, the case is different ; there are numerous observations, and they, with few exceptions go to show that this form of syphilis can rarely be transmitted to the offspring. Whereas MCCRAE (1930) states : " The disease can be carried through as many generations as are able to produce " ; HUTCHINSON (1909) had said : " As to inheritance in the third generation, I am absolutely incredulous." THOMSON (1925) remarks, " The transmission of syphilis to a third generation must be extremely rare, but we have it on the high authority of F. W. MOTT that it does, sometimes, occur." STOKES (1927) states that " A healthy child of a heredosyphilitic parent is the overwhelming rule." FINDLAY (1919) goes further and affirms : " There is no reputed example of transmission even to the third generation. Like other infectious diseases, it is a pure accident of its environment that the child becomes infected *in utero*."

NABARRO (1933), however, has produced evidence which adds greatly to knowledge of third generation syphilis ; he has personal records of sixteen families with syphilis in three generations. Of particular interest in relation to the present topic is the means, apart from the Wassermann reaction, by which the syphilis in the congenitally affected *mothers* was diagnosed or suspected.

In the addendum of cases to his paper it will be found that there were, out of the first sixteen records : one congenitally infected mother with depressed bridge of the nose and looks c.s. ; one with typical c.s. facies ;

one with incisor teeth pegged and notched and history of interstitial keratitis ; one with Hutchinsonian teeth, corneal opacities and history of interstitial keratitis ; one with rhagades about mouth and joint scars ; one in which there were no stigmata but a history of snuffles in infancy ; one which had no syphilitic history or stigmata other than deafness ; one with teeth very suspicious ; one with some narrowing of the incisors ; one with barrel-shaped upper incisors ; one with left upper incisor notched and suggestive and six-year old molars mulberry-like ; one with bossed forehead and R lower canine notched ; and four in whom there was no history of syphilis and no stigmata.

NABARRO appears justified in saying " I have now learned to detect finer points in diagnosis " ; it certainly seems improbable that less experienced persons would see in the great majority of these proved congenital mothers any indication for suspecting congenital syphilis and having a Wassermann or Kahn test performed. The conditions of work in yaws areas render the initial detection of such cases and their final diagnosis infinitely more unlikely, one might almost say, highly improbable.

HUDSON (1932–3) who is making a study of syphilis (bejel) among Euphrates Arabs makes reference to LACAPÈRE'S work among Moroccans and records his own observations in the Syrian desert on the Middle Euphrates. " LACAPÈRE (p. 271) thinks that congenital infection is very common in the Moroccan Arab, 60 per cent. of young Moroccans presenting undoubted marks of congenital syphilis. Our observation of the infants and children of Deir-ez-Zor leads us to the opposite conclusion." He records also that among this population, with a minimum infection of over 50 per cent. as ascertained by Kahn test, keratitis, nerve deafness and notched teeth are rarely, if ever, seen.

Reverting now to the original statement about yaws and syphilis, it seems to be a fallacy to compare the non-venereal disease of childhood, called yaws, with syphilis in general. We ought at least to refrain from comparing it with venereally acquired syphilis ; the comparison should be limited to those forms of syphilis which are non-venereal and which occur in children, namely, the acquired syphilis of early childhood and congenital (transplacentally acquired) syphilis. Since we can discover no sufficient figures as regards the outcome for the acquired form of early childhood, we are driven back to the congenital form as the best available, with which we can reasonably and properly compare yaws. Putting the conclusions we have come to, instead of the textbook antithesis with which we began, namely, yaws never congenital, syphilis congenital, the statement which we now have in its place, accepting fully NABARRO'S figures, is this :—*In yaws* : *congenital transmission very rarely recorded. In congenital syphilis* (*and probably in infantile acquired syphilis*) : *congenital transmission rarely recorded.*

Let us next take a group of boys and girls aged eight, with yaws, and assume that yaws, acquired at the age of eight, will normally act in the same way as venereal syphilis would act if it had been acquired at that age. What then should we expect to find as regards its transmission later to the child *in utero* ? Should we expect that it ought to be transmitted by the mother at the age of fifteen or sixteen to her child ? Even on the too severe analogy of venereally acquired syphilis, I believe we should expect such transmission to be rare. Taking first the males of our eight-year-old group, when they reach the age of marriage they will not be able to infect the females of this group, because the females will be already immune ; neither will they be able to infect non-immune

females, because they themselves, the males, will already have usually passed the infective stage, since the lapse of time factor is of paramount importance even in cases where venereally acquired syphilis is concerned. Thus HARRISON (1931) says: "It is generally agreed that the risk of infection by sexual intercourse becomes very considerably reduced by the end of the second year of infection, and is very slight after five years, though exceptional cases of much longer sexual infectivity have been published. The effect of this is that, on the score of contagion, there is practically no bar to marriage by a syphilitic man after five years."

STOKES says: "Time diminishes the infectiousness of syphilis. After five years few cases are infectious." The same author notes that KEYES placed the chance of infection by the untreated husband as 12 to 1 the first year, 5 to 2 the second year, 1 to 4 the third year, and practically nil the fourth and fifth years.

There is a mass of evidence of this nature, the general trend of which is to show that after the first years of the infection, the chances of even the venereally infected male passing on syphilis to the female, decline with great rapidity; and yaws cases are rarely venereally infected.

Turning now to the females of our eight-year-old group, on marriage they could not infect the immune males, and we should expect to find, owing to the lapse of time, a similar falling off of their chances of infecting non-immune males. But it may be argued that such an infected female might still, though not capable of infecting a non-immune male venereally, be capable of passing on the infection transplacentally to her foetus. On this aspect the evidence points rather to the contrary; HARRISON states: "The transmissibility of the disease certainly becomes less with the age of the mother's infection; thus Belding found that women with infections of more than five years' duration seldom give birth to syphilitic infants." LEES's (1927) evidence on this point is similar, "If the parents suffer from untreated syphilis, the virulence of transmission is always most potent during the first year of infection. It lessens subsequent to this, and a living but weak syphilitic child may be carried to term. By the fifth or sixth years the virulence of transmission slowly lessens, and in many such cases syphilis is no longer transmitted."

Therefore, I would suggest firstly, that the available evidence is altogether against the probability of children who acquired syphilis at this age being able to transmit it commonly to the child *in utero* later, and secondly, that in this respect yaws is like syphilis.

We come now to the infinitely more limited number of women who acquire yaws at adult age. The native mother who, having escaped infection in her youth, acquires the disease from her child, would nevertheless, at first sight, appear to be now in a good position to transmit the disease at her next pregnancy. If the next pregnancy were in a year's time, it is probable that she might do so, but in fact her next pregnancy, if there is one, may, among many native tribes, not be in the next year nor yet in the year after that, owing to the tribal customs and regulations in regard to this matter; here again the lapse of time factor in transmission comes into operation, so that her chance of transmitting would, on the analogy of venereal syphilis, be much diminished by the time her next child was *in utero*.

It will be seen therefore, that the search for instances of congenital transmission of yaws is likely to be rewarded by success among a very limited number of exceptional females, if they are reared in yaws

endemic areas ; it is thus not difficult to understand that such transmission may be a fact, and that it may be occurring in all of those few cases in which it is actually possible, and yet very rarely be recorded. A failure to encounter frequently a case of transplacental transmission in yaws need therefore hardly surprise us ; we are looking for a condition which a study of the epidemiology of the disease proves to us must be rare. The fact that we have not found it cannot be regarded as justifying us in denying the actual occurrence of transmission of yaws from the mother to the child ; still less does it justify our making the assumption that such congenital transmission is impossible in yaws.

The arguments in this section have by some, *e.g.*, VAN NITSEN (1933), been interpreted as intended to prove that yaws is, in fact, congenitally transmitted ; they were not intended to prove more than that we do not yet know whether it is so transmitted or not. If, moreover, we were in a position to affirm now, absolutely, that yaws is *never* transmitted transplacentally, and we are far from that position yet, it would even then be inadmissible to proceed direct to the conclusion that yaws and syphilis are different diseases, due to different parasites ; it would be incumbent upon us to prove that this lack of placenta-passing capacity was inexplicable on any other grounds such as race, climate, epidemiology and general environment. VAN NITSEN cites and formally tabulates a single case of Dr. MATTLET'S, *" observation d'un intérêt capital"* to prove that yaws is not transmitted transplacentally. The mother, in full yaws eruption, gave birth to a healthy child ; the proof given of non-transmission is the Wassermann++ in the mother and 0 in the child, both tested ten days after the birth. Now this observer may be perfectly correct in saying that the child did not inherit yaws, but he omits to prove it ; he fails to mention two facts on which syphilologists are fairly well agreed : first that a congenital syphilitic child may not become Wassermann-positive till much later than ten days after birth, and second, that no one would accept a single negative test as sufficient to exclude syphilis, whether in a child of ten days or anyone else.

II. *Yaws* : *primary sore extragenital.* *Syphilis* : *primary sore usually genital.*

LACAPÈRE (1932) points out that among natives, syphilitic venereal chancres are rarely seen, and that the great number of the primary lesions are extragenital. It is of interest to note what this writer calls the three great characters of the syphilitic chancre among natives : " Il est ordinairement méconnu, son siège est souvent *extragénital* et il se rencontre fréquemment chez l'enfant."

HUDSON has never seen a venereal chancre among the thousands of patients he has examined in the Arab endemic-syphilis area referred to previously.

The extragenital site of the primary lesion of yaws has, therefore, no value as a differential point, by which to distinguish yaws from syphilis.

III. *Yaws* : *typical yaw pathognomonic, furfuraceous and plantar lesions characteristic.* *Syphilis* : *seldom imitates framboesia.*

The diversity of the lesions of the primary and secondary stages of yaws have been emphasized from the early times. MAXWELL (1839) wrote : " It is well known that the whole children on a plantation may be inoculated from a favourable case of yaws, and that the disease will

present as many shades of difference as there are peculiarities among the persons affected." The early experiments of CHARLOUIS (1881) and others bring out the great variations which may occur, and recent experimental workers like SELLARDS, LACY and SCHÖBL (1926) have also shown this.

There are, further, certain observations which prove that even in venereal syphilis important differences exist in the secondary eruption as between the white and the coloured patient, even when the latter is civilized and wears clothes. STOKES points out that the annular secondary syphilide, a form of eruption relatively rare in white patients, is very common in the American negro.

HAZEN (1914) mentions five varieties of syphilides seen among American negroes much more commonly than in other races in America. " The first is the follicular variety, in which the lesions are very small, and situated at the hair follicles ; the second is the annular kind . . . the third is the frambesiform. . . ."

ZIMMERMANN (1921) points out that his observation confirms FOX, GILCHRIST and HAZEN in regarding the annular papular syphilide as a most striking peculiarity in negro syphilis. GOURLEY (1924), in describing venereal diseases among Indian women and speaking of the types of secondary eruption says : " One, the papulo-pustular type needs special mention. It is not infrequently so pustular as to make one stand back and enquire about the possibility of *smallpox*." These and similar observations suggest that we should find even greater differences under more primitive conditions of life ; it is necessary therefore to study the eruption of secondary syphilis in native children with extragenital chancre and living unclothed in similar rural areas, in order to obtain a just comparison with yaws.

The furfuraceous lesions are probably thus emphasized because they look more conspicuous on the native skin, where the branny scales are seen against a dark background.

The differential point about the lesions of the feet, is one which should be taken in conjunction with a consideration of the effects of pressure and injury, in causing localization of a syphilitic eruption. TAYLOR (1930) notes that in all stages of syphilis there is a tendency for the lesions to appear at sites of injury, *e.g.*, mucous patches and glossitis of smokers, squamous syphilides on palms of manual workers, gumma of frontal bones of Mohammedans—from striking forehead during worship. For the same reason that the forehead of the syphilitic Mohammedan shows lesions not to be found in non-Mohammedan, it is probable that the lesions of the bare feet of the syphilitic native will differ from those of a well-shod European adult.

IV. *Yaws* : *mucous membranes not affected. Syphilis* : *mucous membranes affected.*

As regards the yaws side of this statement, MAXWELL long ago expressed his disagreement with it in the following remarks on the eruption of yaws :—" Mr. Mason, who writes a sensible Essay on yaws, has fallen into error in supposing ' the mucous tissues incapable of producing yaws tubercle '." CHARLOUIS described confluent tubercles in the nostril, on the septum, ala and floor. We have also the observation of HUTCHINSON that while he was in Ceylon he found, in cases produced as typical parangi, that there were present symmetrical filmy sores on the tonsils just like those of syphilis. In more recent times we may quote from CASTELLANI (1922) writing of lesions of the

mucous membranes : " These are not very common, but small granulomatous nodules may develop at the base of the tongue, as may whitish patches like syphilis leukoplakia. Small granulomata may form on the nasal mucous membrane, and also on that of the vagina." CALLANAN (1925) records secondary lesions on the tongue.

Turning now to the other side of the statement, namely, *Syphilis* : *mucous membranes affected*, HUTCHINSON says that mucous patches are very often superficial and almost painless, MACLEOD (1920) states that erosions of mucous patches do not as a rule give rise to subjective symptoms and both he and STOKES emphasize the importance of mouth irritants such as alcohol and tobacco in producing and perpetuating such lesions.

ZIMMERMANN, it may be noted, found secondary lesions in the mouth and pharynx to occur in 42·1 per cent. of white patients, as compared with 27·2 of the negro patients in his series of cases. He refers to the mutually contradictory statements of HAZEN and BAETZ on this subject, and also to the observations of CARTER, who did not observe a single mucous patch in two hundred and thirty-one coloured syphilitics, while such lesions occurred in twenty-one of a similar number of white patients. It appears probable that, if there is a smaller percentage among adult negroes than among adult whites, the reason may be sought partly in a relative absence of causes of injury and irritation of the mucous membranes in negro patients.

If we admit that mucous membrane lesions of the mouth are determined by irritants, we should not expect such lesions to be common in yaws children because these are not subjected to such irritations of the mouth, as tobacco and alcohol, which are recognized by all syphilologists as especially predisposing to lesions of the mucous membranes of the mouth.

The evidence thus shows that it is not correct to say that in secondary yaws the mucous membranes are not affected, and that it is equally incorrect to suggest that the mucous membranes are always affected even in secondary venereally acquired syphilis. If we are seeking to institute a comparison between yaws and syphilis, we require to know how the mucous membranes are affected in native children of the tropics who acquire syphilis with an extragenital chancre. Such a group would appear to be the only fair one for comparing syphilis with yaws in children.

V. *Yaws* : *itching common. Syphilis* : *itching rare.*

VI. *Yaws* : *alopecia not known. Syphilis* ; *alopecia may occur.*

Such evidence as exists on these points is contradictory and hardly of use in diagnosis.

VII. *Yaws* : *eyes unaffected. Syphilis* : *iritis common, choroiditis and retinitis rare.*

The iritis incidence presents anomalies for which the explanation does not appear obvious. As far as yaws is concerned, some cases have been recorded from endemic areas ; even among the Fijians, who were not supposed to suffer from syphilis, there is recorded the occurrence of occasional cases.

As regards its frequency in syphilis, there are various statements ; thus HUTCHINSON says at one time that iritis is fairly common, but later says that he had not seen a case for several years. He states : " When the

secondary eruption is at its height, or just when it begins to decline, there occurs in exceptional cases an inflammation of the eye; the iritis, when it happens, is usually symmetrical." McCRAE says iritis is common in syphilis three to six months after the chancre. STOKES, however, writes "Iritis is usually a late secondary; the incidence in our series did not exceed 3 per cent. in the general run of cases; it seems to be more frequently an accompaniment of severe infection." ZIMMERMANN found only four cases of iritis among two hundred and twenty-eight cases of white patients with early secondary syphilis, whereas there were thirty-six cases of acute iritis among two hundred and seventy-nine black patients, and he notes that in seventeen of them it was associated with follicular syphilides. He states that ATKINSON found eleven cases of iritis among one hundred negroes with primary and secondary syphilis. In the tertiary stage he found the negro more prone to iritis than the white; of forty cases in which this occurred as an isolated lesion, or in association with other tertiary lesions, twenty-nine were coloured patients. It is possible that further study of iritis in natives in their own countries may throw light on this question.

Up to the present, among primitive yaws populations, there has been relatively little ophthalmic investigation.

VIII. *Yaws: visceral lesions absent. Syphilis: visceral lesions occur, i.e., pericellular cirrhosis, gumma of liver and kidneys, etc.*

LACAPÈRE, in summing up the differences which distinguish the syphilis of natives of the French Colonies both in the Far East and in North Africa from European syphilis, says that one of the characteristics of the former is the great rarity of visceral lesions. GOUGEROT (1932) discusses the peculiar evolution of colonial native syphilis, and he too emphasizes the rarity of visceral lesions in this native syphilis. GLÜCK (1904) studied endemic syphilis in Bosnia and Herzogovina, where there was a great tendency to extragenital infection during infancy and childhood; he noted as one of the peculiar characters of this type of syphilis that there was comparative infrequency of visceral syphilis.

Now if we permit ourselves to use the absence of visceral lesions in yaws as a fact which entitles us to declare that yaws and syphilis are different diseases, we encounter a difficulty. We cannot argue in this way without admitting that the endemic syphilis of Bosnia and Herzegovina, where children acquire the diseases by extragenital chancre, and also the colonial syphilis of the French, and that of the Arabs of the Euphrates described by HUDSON, are equally not syphilis. But, as we shall see, all the evidence obtained from the observation of Europeans who have contracted syphilis from natives in the tropics, goes to prove that the colonial syphilis is not to be distinguished in any way in its effects on these Europeans, from syphilis contracted venereally from Europeans.

Yaws, as regards its visceral lesions, ought properly to be compared with syphilis in the tropics occurring among children who have acquired it by extragenital chancre, and the evidence suggests that, when this is done, little difference may be found.

IX. *Yaws: nervous system never seriously affected. Syphilis: nervous system prone to infection, tabes, G.P.I.*

Very different figures are given by various observers of the incidence of tabes and paresis in European syphilis.

There are numerous records which suggest strongly that occupation, race and the character of the secondary eruption, are some of the

factors which determine the incidence of these two sequelae of syphilis. OSLER and MCCRAE (1928) pointed out that the civilized peoples are those who get paresis, and further, that it affects men much more frequently than women. LACAPÈRE, in Morocco, considers it probable that it is what he calls " intellectual trauma " which determines paresis in educated Europeans. The evidence of STOKES, MOORE (1921) and ZIMMERMANN goes to prove that American negroes suffer much less from neurosyphilis than do whites ; STOKES writes : " The now well established clinical observation that patients who develop marked cutaneous symptoms are relatively immune from neurosyphilis . . . "; HARRISON (1931a) refers to the same phenomenon in discussing treatment.

Having seen that the three factors, occupation, race and character of the eruption, appear to have importance in relation to the development of paresis and tabes, let us turn from syphilis as it occurs among Europeans, Americans and American negroes, and consider it as it occurs among native peoples in their own lands.

The figures as regards paresis and tabes in syphilis in the natives of tropical and subtropical countries are remarkable. BAETZ (1914) did not find a case of tabes and only one case of paresis in twenty thousand admissions of negroes in the Canal Zone. FLETCHER (1922), who worked in Malay, says that it is the experience of most writers in the tropics, that symptoms of early involvement of the nervous system are uncommon in natives, and that tabes and general paralysis are comparatively rare, at any rate among the native population. HARPER-NELSON (1931) records that in Lahore, during twelve years in charge of sixty medical beds, he saw only two cases of tabes dorsalis and that one of these had European blood, and only one case of G.P.I., and that an Anglo-Indian. Of particular interest in relation to this question are the Uganda figures, because there, among the Baganda people, syphilis is said to be very rife, and congenital syphilis to constitute a grave problem. COOK (1931) says : " In Uganda it has been an amazing thing to me to see how few cases there were of locomotor ataxy and dementia paralytica. I have always tried to take a careful interest in nerve syphilis. I must have seen considerably over one hundred thousand cases of syphilis, but I do not remember seeing a single case of locomotor ataxy or G.P.I. in Uganda." COIA (1931) states that in British Guiana, with one hundred thousand negroes and one hundred thousand Indian immigrants, there have been in ten years two cases of G.P.I. and one of tabes. DECROP (1932) found only two cases of tabes and two of G.P.I. in five years among eighty-four thousand syphilitics in Tangiers.

LEVADITI and MARIE (1914) explain this fact, which has impressed so many observers, as due to difference in strain, suggesting that the *Spirochaeta pallida* producing general paralysis differs biologically from that of cutaneous and mucous syphilis ; they call the former the neurotropic variety ; but the evidence of FLETCHER, COOK, HARRISON and others as regards the effects on Europeans does not lend support to this explanation. LACAPÈRE cites three hundred and forty-three cases of Europeans who contracted syphilis from native women in the French African Colonies ; in all these the syphilitic infection behaved just as it does in cases contracted in France.

From the above records it is clearly impossible to distinguish yaws from syphilis as it affects natives of the tropics by the tabes and G.P.I.

incidence. Yet, as noted, the clinical evidence points to syphilis in natives of the tropics being the same disease as that of Europeans and due to the same spirochaete.

X. *Yaws: no endothelial proliferation as in syphilis. Syphilis: endarteritis obliterans of viscera, cerebral thrombosis.*

Since in some yaws endemic areas where venereal infection rarely appears to be present, aortitis, aneurysm and various plegias are yet common, we must either conclude that these lesions have a different pathology from those of syphilis, or else admit that in yaws, just as in syphilis, endarteritis and thrombosis occur.

A further point to be considered while dealing with this question of endothelial proliferation is the histopathology of the gumma. Gummatous lesions of the skin and subcutaneous tissues are usually held to be very numerous in yaws endemic areas. The gumma of syphilis is considered by most observers to involve endarteritis as a precursor of necrosis. MALLORY (1925) says the term "gumma" in syphilis is practically restricted to those tertiary lesions in which necrosis has taken place as a result of obliterating endarteritis. STOKES writes of the cutaneous syphilitic gumma: "In the pathology of these lesions one sees the granuloma of syphilis most typically portrayed—giant cells, the lymphocytic infiltration, some epithelioid and fibroblastic proliferation, peripheral obliterative endarteritis of the finer capillaries and arterioles, and central softening and necrosis."

If we accept the general testimony that gumma of the skin and subcutaneous tissue is common in yaws, then we are obliged either to admit that obliterative endarteritis does in fact frequently occur in yaws, or else to postulate that the histopathology of the cutaneous gumma of yaws is entirely different from that of the cutaneous gumma of syphilis.

XI. *Yaws: better resisted, constitutional disturbances slight. Syphilis: attacks constitution, affecting vital structures.*

It is difficult to understand the significance of this statement. The primary lesion of syphilis is in itself commonly a much less troublesome lesion than that of yaws. Most observers will consider the secondary stage of yaws, with its precursor malaise, bone pains and general symptoms, to be at least as constitutionally incapacitating as this stage of syphilis. As for the tertiary stage, a great many people will agree with BRANCH (1907) when he says that if syphilis and yaws are different diseases, then yaws is the worse of the two.

If it is the grave effects on the nervous system, *e.g.*, tabes and general paresis, which are meant by the phrase "affecting vital structures," the reader may refer to heading IX where these nervous system lesions are discussed, and where it is shown that the rarity of these affections in yaws does not distinguish it from syphilis among natives of the tropics. Again, if it is the effects on the viscera which are meant, the reader may be referred to the argument under heading VIII where it is shown that the reported lack of visceral lesions in yaws is paralleled by the reported lack of visceral lesions in syphilis in natives of the tropics. Finally, if the vital structures are the blood-vascular system, changes in which cause the lesions which result in paraplegia, hemiplegia and other plegias, reference to them will be found under heading X where it is noted that such lesions are common in yaws endemic areas.

XII. *Yaws: does not respond to mercury. Syphilis: responds well to mercury.*

There is evidence from the earliest times which shows that mercury benefits yaws, just as there is evidence that the results of mercury treatment of syphilis may be extremely disappointing.

There does not appear to be a single manifestation of yaws which has not been reported by one observer or another in syphilis, so that the tabulations break down at various points. In rejecting any or all of the differential items we must avoid replacing them by others equally fallacious. The introduction of such expressions as yaws ectodermotropic, syphilis mesodermotropic seems hardly likely to clarify the subject. A pathogenic organism may change the site of its activities in the animal body with some suddenness and for reasons little understood as yet. For example FINKELSTEIN and ORLOW (1931) record that spirochaetes of syphilis inoculated intravenously into rabbits passed the placenta and caused foetal infection, whereas by other methods of inoculation they failed to do so. A further instance is available; RAIZISS and SEVERAC (1932) record that Nicholl's strain of *Spirochaeta pallida* carried on in the rabbit did not infect the animal's brain; when injected into mice it reached the brain of mice though producing an entirely asymptomatic infection: after this passage through mice the spirochaete had acquired and retained the capacity of reaching and infecting the brain of rabbits when inoculated in the usual way; it had thus acquired neurotropic properties. Without the use of animal experiments we have evidence of even more direct "tropism." STOKES reports a family of four persons all infected with the same strain of spirochaete: the father and one son had highly resistant neurosyphilis, while the mother and other son had quiescent benign infections. It is difficult to understand how syphilitic spirochaetes which show such predilection for the nervous system, as in two of these cases, can be classified as mesodermotropic.

In conclusion it seems reasonable in our present state of knowledge, without claiming that any final scientific proof of unicity exists, to take the morphology, staining, serological and therapeutic tests as pointing to yaws and syphilis being due to the same organism; on this basis we expect much more convincing arguments than those tabulated, before rejecting the evidence of these tests.

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KALA AZAR.

Gimeno Ondovilla (Antonio). Contribución a la epidemiología del kala azar. [**The Epidemiology of Kala Azar.**]—*Trabajos.* Madrid. 1933. Mar. 31. Vol. 2. No. 12. pp. 26–27. With 1 fig.

Seven cases of kala azar have been observed by the author in Spain in 1932. Two cases in children were from Madrid and five cases, of which one was in an adult 27 years of age, were seen in Seville. In this town two of the patients were in one house, another in an adjoining one, while the other two were not distant more than 30 and 60 metres respectively. This quarter of the town was a particularly insanitary one. In the houses of four of the patients dogs lived. An examination of 76 dogs from the district revealed leishmania infection in 5, while of 495 cats examined one is said to have been infected, the parasites, however, being extremely rare. [If this statement regarding the cat is accepted, the record is the second of naturally occurring kala azar in this animal, the first having been made in 1912 in Algeria by Sergent Ed. & Et., Lombard & Quilichini.] *C. M. Wenyon.*

Olmer (D.) & Olmer (Jean). Quelques remarques sur le kala-azar autochtone de l'adulte. [**Indigenous Kala Azar in France.**]—*Marseille-Méd.* 1933. Mar. 5. Vol. 70. No. 7. pp. 341–348. [16 refs.]

It is becoming increasingly evident that kala azar may be acquired by adults in the South of France as well as by children. The authors mention the records of a number of cases and, for the use of local medical men, give a brief account of the methods employed for arriving at a diagnosis. *C. M. W.*

d'Oelsnitz. La pigmentation et le " masque " du kala-azar autochtone de l'adulte. [**Pigmentation in Kala Azar in France.**]—*Bull. Acad. Méd.* 1933. July 4. 97th Year. 3rd Ser. Vol. 110. No. 26. pp. 35–37.

The author has had experience of about 60 cases of kala azar in children in the South of France and of 8 cases in adults of which 5 were undoubtedly autochthonous cases. In this paper attention is drawn to the fact that pigmentation of the skin never occurs in children while it does in adults, thus justifying the term kala azar. The distribution of the pigment on exposed parts of the body and its butterfly distribution on the face are emphasized. On unexposed parts the natural pigmentation of certain areas is intensified. Of the 8 adult cases one showed no pigmentation. *C. M. W.*

Fabri (Giuseppe). Osservazioni sopra un caso di leishmaniosi ribelle alle cure e guarito dopo aver superato una infezione tifica. [**An Obstinate Case of Kala Azar clearing up after an Attack of Typhoid Fever.**]—*Policlinico.* Sez. Prat. 1933. Apr. 10. Vol. 40. No. 15. pp. 563–566. With 3 charts.

A child, six years of age and suffering from kala azar, had failed to respond to treatment with antimony tartrate, 80 centigrams of which had been given, when its condition suddenly became worse. A spleen puncture showed that leishmania were still present. On carrying out a

blood culture it was found that the child had contracted typhoid fever from which it recovered in four weeks. At the same time the general condition improved till finally it became evident that the typhoid infection had brought about a cure of the kala azar. *C. M. W.*

Walker (J. H. C.) & Gibson (C. C. G.). **Leishmaniasis (Kala-Azar) in an Adult contracted in Malta.**—*Jl. Roy. Army Med. Corps.* 1933. June. Vol. 60. No. 6. pp. 449–454. With 1 fig.

A detailed account of a case of kala azar in a soldier aged 22 in which the disease was undoubtedly contracted in Malta. The case is of interest in that the infection was refractory to neostibosan but responded at once to injections of tartar emetic. During the course of neostibosan which did not check the disease, the patient was treated for a short time with a liver preparation in an attempt to combat the anaemia. There was an immediate red cell response but also a big increase in the white to red cell ratio. On discontinuing the liver preparation there was at once a fall in the number of red cells. *C. M. W.*

Sur (S. N.) & Neogi (S. K.). **"Novostiburea" in the Treatment of Kala-Azar.**—*Indian Med. Gaz.* 1933. May. Vol. 68. No. 5. pp. 273–275.

The paper records the treatment of 27 cases of kala azar by either intravenous or intramuscular injections of novostiburea. The drug is of low toxicity and can be administered if desired every day. It produces no unpleasant symptoms. In the cases recorded there was rapid cessation of fever and disappearance of symptoms. In 15 cases which completed treatment the average number of injections was 9, while in 4 adult cases the average quantity of drug used was 2·35 gm. In a foot-note to the paper the editor of the journal notes that the drug was tested at the Calcutta School of Tropical Medicine. Its low toxicity was reported upon, but it was found to be less effective than other drugs.

C. M. W.

Giardina (Agostino). La cura della leishmaniosi interna col tartrato di sodio e d'antimonio. [**Treatment of Kala Azar with Sodium Antimony Tartrate.**]—*Riv. Sanitaria Siciliana.* 1932. Dec. 15. Vol. 20. No. 24. pp. 1797–1798, 1801–1804. With 1 chart. [13 refs.] English summary (4 lines).

Since March 1929 there have been treated as outpatients at the children's clinic at Palermo 130 cases of infantile kala azar. The method of treatment has been two intravenous injections a week of a 1 per cent. solution of sodium antimony tartrate. Of the 130 cases, 79 continued the course of treatment to the end and were cured, while the remainder for one reason or another abandoned it. The advantage of being able to treat children as outpatients is obvious. *C. M. W.*

Gimeno Ondovilla (Antonio). Contribución al diagnóstico del kala-azar. [**The Diagnosis of Kala Azar.**]—*Trabajos.* Madrid. 1933. Jan. 31. Vol. 2. No. 8. pp. 30–31.

The author concludes, from the study of 7 cases of kala azar in Spain and a number of controls, that the serological reactions for kala azar

and the administration of a provocative dose of neostibosan to cause parasites to appear in the blood, are tests which are of value in diagnosis when spleen puncture cannot be performed. *C. M. W.*

D'Oelsnitz & Faure-Brac. Le dépistage du kala-azar. [**Diagnosis of Kala Azar.**]—*Bull. Acad. Méd.* 1933. Feb. 28. 97th Year. 3rd Ser. Vol. 109. No. 9. pp. 265–268.

The paper is a discussion of the relative value of the various laboratory procedures which may be applied to the diagnosis of kala azar. Apart from actual discovery of the parasite by spleen, liver or bone puncture the antimony test appears to be the most reliable.

C. M. W.

Mathewossjan (Sch. T.) & Zaturjan (A. T.). Experimentelle Infektion des armenischen Hamsters *Cricetulus migratorius* mit *Leishmania donovani*. [**Experimental Infection of** *C. migratorius* **with** *L. donovani*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Apr. Vol. 37. No. 4. pp. 190–193.

In recording the susceptibility to inoculations with *Leishmania donovani* of the Armenian hamster, *Cricetulus migratorius*, the authors note that during recent years, 1928–1932, there had been registered, mostly in Erivan, 85 autochthonous cases of kala azar in human beings and one case in a dog. The hamster in question is a small animal which has the habits of the ordinary house mouse and is found in all the houses of Erivan. Of 32 inoculated with cultures of various ages 15 became infected and of 4 inoculated with the tissue forms of the parasite all were infected. The longest interval between inoculation and examination in a positive case was 128 days. *C. M. W.*

Giraud (Paul) & Cabassu (Henri). Sur la valeur des procédés de laboratoire pour le diagnostic de la leishmaniose canine naturelle. [**The Diagnosis of Canine Leishmaniasis.**]—*Ann. Inst. Pasteur.* 1933. Apr. Vol. 50. No. 4. pp. 539–549.

In this article the authors discuss the value of the various procedures for the diagnosis of kala azar as applied to dogs. Apart from the discovery of the parasite, which is most readily done by the examination of smears made from cutaneous lesions, if such occur, or by performing bone puncture to obtain marrow, preferably from the anterior end of a rib, the formol gel reaction gives the most reliable information. In fact the various procedures have much the same values as they have in the diagnosis of the human disease. *C. M. W.*

Rivera (J.). Nota sobre la leishmaniosis canina en Madrid. [**Canine Leishmaniasis in Madrid.**]—*Trabajos.* Madrid. 1933. Apr. 15. Vol. 2. No. 13. p. 30.

A previous examination of 200 dogs in Madrid in 1914 did not lead to the discovery of a single case of leishmania infection. The examination by the author of a similar number of stray dogs destroyed by the municipal authorities between February 10 and March 20, 1933, has revealed leishmania infection in 11. The general condition of the infected dogs as regards emaciation, skin lesions, and size of the spleen corresponds with what is known of kala azar in these animals.

C. M W.

Sarnelli (Tommaso). Presenza di leishmaniosi mucocutanee sugli altipiani dell'Arabia Sud-Occidentale. (Nota preventiva.) [**Mucocutaneous Leishmaniasis in the Uplands of South-west Arabia.**]—*Arch. Ital. Sci. Med. Colon.* 1933. Mar. 1. Vol. 14. No. 3. pp. 227–228.

At Sana', the capital of the Yemen district of Arabia, where oriental sore is common, the author has seen three cases of mucocutaneous leishmaniasis. In two the nasal mucosa was involved, and in one the labio-oral mucosa. Two cases of recently treated nasal mucosal lesions were also seen. Of kala azar two cases were diagnosed by microscopic examination. One was in a child five years of age and the other in a child of twelve. The author mentions native remedies for the mucocutaneous lesions which he thinks may be efficacious as the terrible tissue destruction, seen in S. American cases, is not seen here. He recognizes, however, that the leishmania of Arabia may be less virulent than that of S. America. [It seems, however, to the reviewer that these relatively slight involvements of the mucosae in endemic centres of oriental sore which are reported from time to time, represent merely extensions of cutaneous lesions and are of quite a different nature to the very serious and lasting disease of S. America.] *C. M. W.*

Muir (E.) & Chatterjee (S. N.). **A Rare Type of Dermal Leishmaniasis.**—*Indian Med. Gaz.* 1933. Apr. Vol. 68. No. 4. pp. 211–212. With 5 figs.

The case described is that of a man with a six years' history of erythematous eruptions with annular lesions, thickening of the skin and nodule formation over the greater part of the body. A persistent diagnosis of leprosy was made, but eventually the condition was found to be due to leishmania infection of the skin. It is significant that about a year before the skin condition commenced on the abdomen the patient suffered from a fever with enlargement of the spleen from which he recovered without treatment. *C. M. W.*

Hayward (E. W.). **Notes on Berberine Sulphate in Oriental Sore.**—*Indian Med. Gaz.* 1933. May. Vol. 68. No. 5. p. 265.

This short note gives some details of the treatment with berberine sulphate of between three and four hundred cases of oriental sore in Rajputana. In a fair proportion of the cases leishmania was found, but it is noted that owing to pressure of work it is not possible to search for parasites in every case. The number of injections of berberine sulphate varied, but it appears that all cases which received five or more injections were cured. The records show that the injections are sufficiently painful to drive away a large number of patients, but the treatment, if persisted in, is a certain cure. *C. M. W.*

Laqueur (B.). Ueber Chemotherapie der Leishmaniosis cutanea. II. Mitteilung. [**Treatment of Oriental Sore.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Apr. Vol. 37. No. 4. p. 194.

Referring to the method of treatment of oriental sore with camphor ointment (see this *Bulletin*, Vol. 29, p. 873) the author notes that in certain very anaemic patients there is poor response and delayed

recovery. In such cases treatment with tonics of arsenic, strychnine and other drugs should be undertaken, while the granulations are stimulated with balsam of Peru or silver nitrate. *C. M. W.*

MORETTI (Egisto). Su di un raro caso di bottone d'oriente unico palpebrale, simulante un epitelioma. [**Oriental Sore of the Eyelid.**]—*Riv. Sanitaria Siciliana.* 1933. Feb. 15. Vol. 21. No. 4. pp. 284, 287–290, 293–6, 299. [10 refs.] English summary (5 lines).

A record, with a lengthy discussion on differential diagnosis and other matters, of a case of oriental sore of the eyelid in an adult, fifty-five years of age, an inhabitant of Catania. *C. M. W.*

MONTFORT (R.). Sur un nouveau cas de bouton d'Orient observé à Beni Ounif (Sud oranais). [**Oriental Sore in Beni Ounif (Southern Oran).**]—*Arch. Inst. Pasteur d'Algérie.* 1933. Mar. Vol. 11. No. 1. pp. 24–25.

In 1932 HORRENBERGER recorded two cases of oriental sore from Beni Ounif in Southern Oran where the disease had not hitherto been noted. The author now records the third case from the same place. *C. M. W.*

MONACELLI (M.). Su di un focolaio di Leishmaniosi cutanea endemica in Abruzzo. [**Endemic Focus of Oriental Sore in Abruzzo.**]—*Policlinico.* Sez. Prat. 1933. June 26. Vol. 40. No. 26. pp. 1007–1010. With 5 text figs.

A description of a number of cases of oriental sore from certain districts of Abruzzo, demonstrating the endemicity of the disease in the Province of Teramo in Italy. *C. M. W.*

GONZALEZ (Senen) & TOSCANO (Juan Mo.). Contribución al estudio del kala-azar en la provincia de Jaén. [**Kala Azar in the Province of Jaén (Spain).**]—*Medicina Países Cálidos.* Madrid. 1933. Mar. Vol. 6. No. 2. pp. 133–137. [45 refs.]

The record of a case of kala azar in a child 18 months old from Castellar de Santisteban in the Spanish Province of Jaén. It is noted that since the record of the first case of kala azar from Spain in 1912 cases have been described from all districts of the country. *C. M. W.*

D'OELSNITZ & GAUTSCHI. Un nouveau cas autochtone de kala-azar de l'adulte rapidement guéri par le traitement stibié. [**An Indigenous Case of Kala Azar.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1933. Mar. 20. 49th Year. 3rd Ser. No 9. pp. 344–348. With 1 fig.

The record of a case of kala azar in a woman, forty-two years of age, in which the disease appears to have been contracted in the South of France, probably in Nice. A cure was effected with neostibosan *C. M. W.*

CARTIA (Giovanni). Due casi di leishmaniosi interna nell'adulto.—*Riv. Sanitaria Siciliana.* 1932. Oct. 1. Vol. 20. No. 19. pp. 1371–1376. English summary (4 lines).

AMOEBIASIS AND DYSENTERY.

Amoebiasis.

Meleney (Henry E.) & Frye (William W.). **Studies of *Endamoeba histolytica* and Other Intestinal Protozoa in Tennessee : V. A Comparison of Five Strains of *E. histolytica* with Reference to their Pathogenicity for Kittens.**—*Amer. Jl. Hyg.* 1933. May. Vol. 17. No. 3. pp. 637–655. With 1 graph & 1 plate. [13 refs.]

This study was undertaken because of the differences in the clinical manifestations of *E. histolytica* infection in two communities in Tennessee, in one of which a high incidence of infection was associated with little evidence of active amoebic dysentery, and in the other a lower incidence but an acute amoebic dysentery epidemic.

" 1. A study has been made of the relative pathogenicity for kittens of two strains of *Endamoeba histolytica* from the hill country of the Eastern Highland Rim of Tennessee and of three strains from the lowland of West Tennessee. Three hundred and sixty-four kittens were inoculated by rectum or by ileum with cultures of these strains.

" 2. In the first series of rectal injections, performed when the strains had been in culture between 17 and 132 days, the lowland strains from acute cases produced a much higher incidence of infection than did the two hill strains. The lowland carrier strain produced an incidence of infection about equal to the chronic hill strain.

" 3. The second series of rectal injections, performed with four of the strains when they had been in culture between 253 and 262 days, gave about the same incidence of infection with all strains. There was some increase with the hill carrier strain and a decrease with the two lowland strains from acute cases.

" 4. Injection of cultures directly into the ileum gave a higher incidence of infection with all strains than injection by rectum.

" 5. With each of the two hill strains a few kittens known to have been successfully infected showed no macroscopic lesions at autopsy, whereas none of the kittens successfully infected with the three lowland strains were without macroscopic lesions at autopsy.

" 6. Most of the kittens successfully infected with the hill strains showed only a few small lesions in the colon, whereas most of those infected with the lowland strains showed moderate or intense pathology.

" 7. When the duration of the infection in each kitten is considered, the above differences in pathology still hold true. The lesions produced by each of the lowland strains apparently progressed with greater rapidity than those produced by the hill strains.

" 8. These observations seem to indicate that strains of *E. histolytica* from different localities may show differences in the incidence of infection and in the amount of pathology produced in experimental animals.

" 9. A somewhat higher incidence of infection in kittens was obtained with culture transplants two or three days old than with older transplants." *H. M. Hanschell.*

Johnstone (H. G.), David (N. A.) & Reed (A. C.). **A Protozoal Survey of One Thousand Prisoners with Clinical Data on Ninety-Two Cases of Amebiasis.**—*Jl. Amer. Med. Assoc.* 1933. Mar. 11. Vol. 100. No. 10. pp. 728–731.

In a protozoal survey of 1,000 inmates of San Quentin prison (California) infestation with *E. histolytica* was found in 9·2 per cent.; 78

of the 92 men with *E. histolytica* infestation lived in or had visited areas of well known amoebic endemicity and 36 of these had lived in tropical regions ; 52 had experienced notable gastro-intestinal upsets.

H. M. H.

ARNETT (John H.), WENRICH (D. H.) & STABLER (R. M.). **A Survey of 401 College Freshmen for Intestinal Protozoa.**—*Amer. Jl. Trop. Med.* 1933. May. Vol. 13. No. 3. pp. 311–315. [10 refs.]

Of 401 freshmen in a Philadelphia college, 95 per cent. came from Pennsylvania and New Jersey and few had travelled extensively. A single normal stool was examined for each person, both by stained slides and fresh smears in saline and iodine. Stained slides revealed 167 protozoan infestations as against 147 for fresh smears. The combined methods yielded 176. One or more species of protozoa were found in 33·1 per cent. of the students, 4·5 per cent. being carriers of *E. histolytica* ; only one carrier of *E. histolytica* suffered from symptoms which might be attributed to the amoeba. *H. M. H.*

DOUGHERTY (Mark S.), Jr. **Amebiasis a Public Health Problem in the Cities of the Southern United States.**—*Amer. Jl. Trop. Med.* 1933. May. Vol. 13. No. 3. pp. 317–325. [20 refs.]

The epidemiology of amoebiasis is reviewed. A report is given of 396 cases of amoebiasis occurring in the hospitals of 13 southern cities in 1927–1931 inclusive and of 55 cases out of 1,103 patients examined during the past five years. The public health problem consists in proper disposal of human excreta ; adequate protection of water supplies ; encouragement of physicians to report cases of amoebiasis ; and careful investigation of the food handler problem. In the main, however, solving of the " amoebiasis problem " rests with the physicians in private practice. *H. M. H.*

DESCHIENS (R.). Comment concevoir les complications viscérales de l'amibiase. [**The Pathogeny of Amoebic Metastasis.**]—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 178–183.

In this critical review the author once more insists that the sole criterion of the amoebic nature of a visceral manifestation is *parasitological proof* of amoebiasis by demonstration of the dysentery amoeba by means of permanent stained preparations. He points out that this proof is still lacking for " amoebic adenitis, bronchitis, cystitis, nephritis, urethritis, cholecystitis." He maintains that there is as yet no reason to entertain any conception of amoebiasis other than the classic one, that is, an intestinal infection (dysentery or colitis) which by metastasis or direct propagation can set up other visceral complications, generally suppurative. *H. M. H.*

DES ESSARTS (J. Quérangal). Amibiase et parasitisme intestinaux à Brest. [**Amoebiasis at Brest.**]—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 192–200.

This investigation reveals that intestinal amoebiasis in its chronic form and of exotic origin is relatively frequent in the port of Brest. Autochthonous cases are rare, although a number of conditions appear

to favour propagation of the infection. Healthy carriers of dysentery amoeba cysts are also rare, even among those living in close contact with the amoebiasis cases. *H. M. H.*

Titvinidze (I. G.). Zur Diagnostik der Amöbendysenterie. [**Diagnosis of Amoebic Dysentery.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Apr. Vol. 37. No. 4. pp. 175–176.

The author recommends a preliminary washing out of the bowel by rectal clysma of physiological salt solution at 37–38° C. followed by another of 200–500 cc. at same temperature. When passed out it will be found to contain floating flecks of blood stained mucus—washings from the bowel ulcers. These flecks on microscopical examination reveal numerous amoebae. *H. M. H.*

Rocca (Giuseppe Cascio). Un caso di prostatite da *Entamoeba histolytica*. [**Amoebic Prostatitis.**]—*Riv. Sanitaria Siciliana.* 1932. Oct. 1. Vol. 20. No. 19. pp. 1357–1360, 1363–1366, 1369–1371. With 6 figs. English summary (8 lines).

This case of unusual localization of *E. histolytica* was followed up with more care than the majority of instances recorded. A man of 28 years complained of perineal pain, discomfort and a feeling of weight in the anoperineal region. Examination showed an enlarged prostate, and in the fluid expressed vegetative amoebae were seen, with engulfed red cells. The urine showed none, but in the faeces were both vegetative and cystic forms of *E. histolytica*. Rectal injections of both faeces and prostatic fluid were made into kittens. In a week or so the animals suffered from diarrhoea and lost weight, and in the faeces vegetative amoebae were found. Post mortem the changes in the intestinal wall were those of amoebiasis, macroscopically and histologically. The article is illustrated by microphotographs demonstrating the pathological conditions found in the kittens. *H. H. S.*

Simić (Tshedomir). L'infection du chien par l'*Entamoeba dispar* Brumpt. [**Infection of the Dog with** *Ent. dispar*.]—*Ann. Parasit. Humaine et Comparée.* 1933. Mar. 1. Vol. 11. No. 2. pp. 117–128.

Two strains of *Entamoeba dispar* from Skoplje, of which one was accompanied by Trichomonas, were inoculated intrarectally and the vegetative forms of the two strains inoculated *per os*, into a number of puppies.

The animals infected by *E. dispar* alone were rid of that amoeba in 5 to 7 days, while those infected by both *E. dispar* and Trichomonas, were rid of the amoeba in 5 to 7 days and of the Trichomonas in about one month, if they were over one month old. If they were less than a month old, although the amoeba disappeared they succumbed eventually to the Trichomonas infection. The puppies cured of *E. dispar* infection could not be reinfected with that amoeba. Those infected with *E. dispar* were not made ill by the infection. In the animals' gut the amoeba never became haematophagous, and autopsy revealed no changes in the mucous membrane of the large intestine. The author concludes that the puppy up to two months old is the experimental animal of choice for definitely distinguishing *Entamoeba dispar*, a saprophytic amoeba, from *Entamoeba dysenteriae* —the cause of amoebic dysentery. *H. M. H.*

CRAIG (Charles F.) & KAGY (Edwin). **A Study of Complement Fixation in Experimental Amebiasis in Dogs.**—*Amer. Jl. Hyg.* 1933. July. Vol. 18. No. 1. pp. 202–219. [10 refs.]

The authors' experimental studies, here reported in detail, lead them to conclude that complement-fixing (C.F.) bodies are present in blood serum of dogs experimentally infected with *E. histolytica* and can be demonstrated when alcoholic extracts of cultures of this parasite are used as antigens. C.F. bodies are not present in blood serum of dogs free from *E. histolytica* infection. C.F. bodies from *E. histolytica* may be demonstrated in blood serum of experimentally infected dogs as early as three days after colonic inoculation, and the majority of infected dogs will give a positive C.F. within fifteen days after colonic inoculation. Positive C.F. reactions three to five days after colonic inoculation of *E. histolytica* indicate severe and widespread amoebic ulceration of intestine as proven by lesions observed at autopsy. C.F. bodies for *E. histolytica* disappear from blood serum of experimentally infected dogs after recovery from the infection. In dogs experimentally infected with *E. histolytica* the complement-fixation reaction, if positive, is specific for such infection when alcoholic extracts of cultures of this amoeba are used as antigens. *H. M. H.*

[For Craig's last paper on this subject, see page 387, above.]

CRAIG (Charles F.). **Further Observations upon the Complement Fixation Test in the Diagnosis of Amebiasis. An Analysis of the Results of the Test in One Thousand Individuals.**—*Jl. Lab. & Clin. Med.* 1933. June. Vol. 18. No. 9. pp. 873–881. [18 refs.]

The author's own conclusions are that—

Specific complement fixing (C.F.) bodies may be demonstrated in blood serum of individuals infected with *E. histolytica* when alcoholic extracts of cultures of this parasite are used as antigens. Normal individuals or those suffering from other infections or diseases do not give a positive C.F. reaction with such antigens unless there is a coincident infection with *E. histolytica*. The specific (C.F.) bodies disappear from the blood serum following antiamoebic treatment and disappearance of *E. histolytica* from the faeces. In relapsing cases of amoebiasis the C.F. test, which has been negative during the interval of apparent freedom from *E. histolytica*, again becomes positive, in rare instances even before the parasite is again demonstrable in the faeces. Thus a negative reaction, unless repeatedly so for several weeks, does not prove absence of amoebic infection or that antiamoebic treatment has resulted in cure. The time of disappearance of the positive C.F. reaction after treatment resulting in disappearance of *E. histolytica* from faeces varied between three and twenty-eight days. In 86·6 per cent. of cases studied the reaction vanished within fourteen days after cessation of antiamoebic treatment, and in 96·6 per cent. within twenty-one days after cessation of treatment resulting in disappearance of parasites from faeces. Individuals infested with other species of amoebae, or with intestinal flagellates, do not give a positive C.F. with this test unless *E. histolytica* is also present. The C.F. reaction occurs in all stages of amoebiasis but strongest positive results are usually obtained in symptomless "carriers" or in those presenting mild symptoms of infection with *E. histolytica*. In several cases of very acute amoebic colitis the reaction has been doubtful or negative, although in most severe cases it has been positive. The test has proved of value in

diagnosis of cases of amoebic abscess of liver without intestinal symptoms; of cases of apparently healthy *E. histolytica* "carriers," and of cases presenting atypical or mild symptoms of infection; and in the control of antiamoebic treatment. [See also Vol. 28, p. 262.]

H. M. H.

Bacillary Dysentery.

Manzuoli (J.). Epidemia de disentería bacteriana a bacilos Shiga en Las Varillas (Provincia de Córdoba). [**An Outbreak of Bacillary Dysentery in Las Varillas (Córdova).**]—*Semana Méd.* 1933. Jan. 5. Vol. 40. No. 1 (2034). pp. 70–71.

Montoya (D. J.) & Ortiz (L. J.). Una epidemia de disentería bacilar en Las Varillas (Córdoba).—*Ibid.* pp. 71–73.

Sordelli (A.) & Savino (E.). Epidemia de disentería bacilar en Las Varillas (Provincia de Córdoba).—*Ibid.* pp. 73–76.

A description of an outbreak of dysentery from the clinical and bacteriological aspects. The first and second articles deal with the clinical side of the question. There were 30 cases in all, and, though 5 patients died, the general trend of the disease was mild. Many of the patients were young, 2–14 years. Believing that the condition was amoebic, yatren and emetine were given, and it was only when this proved ineffectual that the bacillary nature of the infection was suspected and specimens were sent to the laboratory, and *Bact. dysenteriae* Shiga, was isolated. Serum for treatment was sent by Dr. Sordelli, Director of the Bacteriological Institute. In most cases there was little or no rise of temperature, colic was not severe, and though the stools numbered up to 20 (in one severe case from 35–100) in the 24 hours, the patients were in many instances able to keep at work. In the adults the symptoms were "quite benign." Only the very early cases were severe; 4 children died in a week. The attacks ran a course of 1–15 days after an incubation of 1–5 days. Infection is believed to have been fly-borne. The third article appeared (verbatim) in *Folia Biol.* and was abstracted in *Bulletin of Hygiene*, 1933, Vol. 8, p. 258.

H. H. S.

Wolff (J. W.). Bijdrage tot de epidemiologie der bacillaire dysenterie [**Epidemiology of Bacillary Dysentery.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1933. Vol. 73. No. 9. pp. 514–523. With 3 graphs.

In this article a direct parallel is made out, for the labour population of the plantations of Sumatra, with the experimental results obtained in mouse populations as a result of immigration and emigration. This parallelism, however, applies only to Y-Flexner dysentery and not to Shiga dysentery. Infection in the latter case was ascribed almost solely to the indigenous Batak population of the highlands. Introduction of fresh cases and accessions to the labour force took place continuously from Java to Sumatra until the process was exactly reversed in 1931 with closure of many of the estates. This influx and efflux is reflected, for the period 1925–1932, in the number of cases and the morbidity rates of Y-Flexner dysentery. *W. F. Harvey.*

CASTELLANI (Aldo). **A Little-Known Type of Chronic Colitis (Chronic Metadysentery).**—*Jl. Trop. Med. & Hyg.* 1933. Apr. 15. Vol. 36. No. 8. pp. 109–115. [36 refs.]

The views of the author and his contribution to the differentiation of that group of dysentery bacilli which he has named meta-dysentery bacilli, are well known. In this lecture he refers to the common occurrence of a chronic disease, " not rarely starting in childhood or youth and lasting for many years," which owes its causation to a bacillus of this group. Illustrative cases are described. The agglutination of the blood of 59 out of 91 cases was positive at a dilution of 1 in 80 or over with one or more varieties of the metadysentery bacilli. " A positive diagnosis can be made only by bacteriological methods."

W. F. Harvey.

HOSOYA (Seigo), TERAO (Shuzo) & TAKATA (Shin). **A Method for Purification of Shiga Dysentery Bacillus Toxin and Antigenicity of the Anatoxin derived from Purified Toxin.**—*Japanese Jl. Experim. Med.* 1933. June 20. Vol. 11. No. 3. pp. 153–169. [30 refs.]

The method used for purification was the exotoxin purification method of HOSOYA and MIYATA combined with WILLSTÄTTER'S enzyme purification method and the yield was satisfactory. An antiserum, obtained by using the formalinized toxin (anatoxin), had a comparatively high value but did not precipitate the anatoxin and did not agglutinate Shiga dysentery bacilli. *W. F. Harvey.*

ARCHER (G. T. L.). **Note on a Non-Mannite-fermenting Organism recovered from Two Cases of Dysentery.**—*Jl. Roy. Army Med. Corps.* 1933. July. Vol. 61. No. 1. pp. 55–56.

This organism isolated in Wellington, India, differed from *Bact. dysenteriae* Shiga by fermenting dulcite and from *Bact. dysenteriae* Schmitz by fermenting dulcite and failing to produce indole. The serum of the patients agglutinated *Bact. dysenteriae* Schmitz but no other organisms of the dysentery group. Agglutination tests applied to the organism itself were negative with anti-Shiga and anti-Schmitz sera. *W. F. Harvey.*

KESSEL (John F.) & ROSE (Edythe J.). **Bacteriophage Therapy in Bacillary Dysentery of the Flexner Type.**—*Ann. Intern. Med.* 1933. Mar. Vol. 6. No. 9. pp. 1193–1199.

The controls applied in this series of cases appear to be adequate to meet objections both in regard to being alternate as far as practicable and as regards the use of a phage with sufficiently high lytic potency towards the bacterium isolated from the patients. Twelve cases were treated with bacteriophage in 1930 and their stay in hospital averaged 11·9 days as compared with 10·1 days for the ten controls. Twenty-three cases treated in 1931 had an average stay in hospital of 11 days and 4 deaths as compared with 12·1 days and 3 deaths in the 23 control cases. " These results indicate that the oral administration of bacteriophage as used in this study, produces no marked clinical benefit over the recognized symptomatic care and treatment." *W. F. Harvey.*

Bouffard (G.) & Vaucel (M.). Essai de prophylaxie en Afrique Equatoriale Française des dysenteries bacillaires par la toxine formolée. [**Prophylaxis of Bacillary Dysentery in Tropical Africa by Formolized Toxin.**]—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 154–168.

The authors' experiences lead them to conclude that vaccination with formolized toxin to be efficacious requires as careful a technique as with diphtheria anatoxin. There should be a three weeks' interval between injections. Immunity conferred is strictly specific. They are not able to estimate precisely its value, but note that its employment has been followed by a decrease in mortality among those labour groups frequently infected with Shiga bacillus. Duration of immunity cannot yet be fixed but appears to be long enough to keep the infection sporadic and to avoid epidemic explosions. To prepare an active anatoxin it is indispensable to make use of a very toxic Shiga strain.

H. M. H.

Gupta (B. M. Das). **Fatal Flexner Bacillus Infection in an Anthropoid Ape** (*Hylobates hoolock*).—*Indian Med. Gaz.* 1933. Mar. Vol. 68. No. 3. pp. 138–139.

The history of this monkey is of interest from the following points—its susceptibility to monkey malaria; its refractoriness to human quartan malaria; the presence in its colon of an entamoeba conforming in all respects to *Entamoeba histolytica* of man, but apparently not a tissue-invader; and the fatal infection with an organism corresponding in all particulars to the bacillus of Flexner. *H. M. H.*

Acanfora (Giuseppe). Le lesioni anatomo-patologiche sperimentali da bacillus ceylonensis " A " (B. dysenteriae Castellani-Sonne).—*Riforma Med.* 1933. July 20. Vol. 49. No. 23. pp. 863–864, 867–868.

Berret & Nguyen-ba-Tung (M.). Abcès du foie et collections sous-phréniques. *Bull. Soc. Méd.-Chirurg. Indochine.* 1932. Nov.–Dec. Vol. 10. No. 8. pp. 806–810.

Botreau-Roussel (M.) & Huard (P.). Deux observations d'amibiase cutanée chirurgicale.—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 202–206.

Botreau-Roussel & Huard (P.). Appendicite aiguë grave chez un amibien suivie d'abcès du foie à streptocoques développé sur une ancienne cicatrice d'abcès amibien.—*Bull. Soc. Path. Exot.* 1933. Mar. 8. Vol. 26. No. 3. pp. 405–411.

Botreau-Roussel & Huard (P.). Deux observations d'amibiase cutanée chirurgicale. (2e partie.)—*Bull. Soc. Path. Exot.* 1933. Mar. 8. Vol. 26. No. 3. pp. 411–415. [19 refs.]

Gessner (Hermann B.) A Review of Ninety-Six Cases of Abscess of the Liver.—*New Orleans Med. & Surg. Jl.* 1933. May. Vol. 85. No. 11. pp. 793–796.

Girard (G.). Etiologie des maladies dysentériques à Madagascar.—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 168–171.

Hargrove (M. D.). Treatment of Amebic Abscess of Liver by Aspiration.—*New Orleans Med. & Surg. Jl.* 1933. July. Vol. 86. No. 1. pp. 21–24.

Hiyeda (Kentarô). On Intestinal Amoebiasis.—*Trans. Japanese Path. Soc.* 1932. Vol. 22. pp. 778–781.

Marmo (Achille). Cases of Metadysentery Observed in Erithrea.—*Jl. Trop. Med. & Hyg.* 1933. Mar. 1. Vol. 36. No. 5. pp. 69–74. [51 refs.]

Montel (R.). Adénopathies iliaques dans l'amibiase. (Etude clinique.)—*Bull. Soc. Path. Exot.* 1933. Feb. 8 & 9. Vol. 26. No. 2. pp. 187–192.

Proceedings of the Royal Society of Medicine. 1933. June. Vol. 26. No. 8. pp. 1049–1062 (Sect. Trop. Dis. & Parasit. pp. 59–72). With 1 coloured plate & 1 chart.—Discussion on the Diagnosis of Chronic Diarrhoeas [Hutchison (Robert), Manson-Bahr (P. H.), Norbury (Lionel E. C.), Milligan (E. T. C.), Fairley (Hamilton)].

Sangiorgi (Giuseppe). Contributo alla conoscenza delle dissenterie miste.—(La "Coliamebo blastocistosi").—*Pathologica.* 1933. Feb. 15. Vol. 25. No. 496. pp. 71–74. With 2 figs. [26 refs.] English summary.

Scaffidi (Vittorio), Jr. Degenerazione amiloide del fegato secondaria ad ascesso amebico.—*Policlinico.* Sez. Prat. 1933. May 8. Vol. 40. No. 19. pp. 736–740. With 1 fig.

Resio (Luis Leon). Angiocolitis supurada amebiana.—*Prensa Méd. Argentina.* 1933. May 17. Vol. 20. No. 20. pp. 1104–1106.

Rosebery (Sidney). Dysentery : a Practical Survey of One Thousand Cases in a General Hospital in Egypt, 1918–1919.—*Med. Jl. Australia.* 1933. Apr. 1. 20th Year. Vol. 1. No. 13. pp. 391–402. With 4 charts. [44 refs.]

SLEEPING SICKNESS.

Fairbairn (H.). **Experimental Infection of Man with a Strain of *Trypanosoma rhodesiense* Apparently Susceptible to Normal Human Serum *in Vitro*.—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 251–264. With 1 chart & 1 plate. [10 refs.]

A strain of *T. rhodesiense* was found to be still infective to man after it had been maintained by passage through rats for a period of nearly a year, during which time it had become sensitive to human serum *in vitro*. From this observation it is argued that the trypanolytic power of human serum is no indication of the power of the body to deal with trypanosomes.

The strain in question was isolated from a Kibondo native on 21st February, 1932, and maintained until 31st January, 1933, by passage through a series of 19 rats. The reaction to undiluted normal human serum of the strain from each rat was tested, and the results are shown in a table. The technique adopted was identical with that described by the reviewer and his colleagues (1930), except that the temperature was maintained at 37°C. for 12 hours during the daytime, but, owing to the fact that the incubator had no regulating mechanism, it was allowed to fall to 21°C. during the night. Furthermore, rats were usually subinoculated with the trypanosome-serum mixture at the end of 24 hours to see if the absence of trypanosomes, as shown by microscopical examination, really meant that all the trypanosomes had been killed by the serum.

According to this technique the strain appeared to have lost its serum resistance from the 9th rat passage onwards (*i.e.*, 176 days after isolation). At the 19th rat passage, when it had been isolated 345 days, its serum resistance was tested against 4 tubes of the author's serum. Immediately after the tubes had been put up, 1 cc. of the Ringer-glucose-trypanosome mixture was inoculated subcutaneously into a rat, and 1 cc. into the author's arm. The rat became infected on the 4th day and the author showed trypanosomes in his blood on the 8th day. In none of the 4 tubes containing the serum-trypanosome mixture were trypanosomes discovered by microscopic examination after the second hour, but one of the four rats inoculated with the mixture after 24 hours became infected.

Details are given of the course of the infection in the experimentally infected human being. The first sign of the disease was a lump about the size of an almond at the site of injection on the sixth day; the following day the lump was larger and its borders more diffuse; it was very tender, the centre was a salmon-coloured patch about the size of a sixpence, and it was surrounded by a lilac areola. The same day the temperature rose to 100·2°F. Trypanosomes were first found in the blood on the 8th day; a course of Bayer 205 was then given and the patient recovered.

Fairbairn then passes to a discussion of the significance of these observations. He begins with the following quotation from a paper of the reviewer and his colleagues: "It seems to us incredible that our laboratory strain of *T. rhodesiense* which, as we have shown, is killed by normal human serum, or plasma, *in vitro* at 37°C. within a few hours . . . could infect man"; and later: "The pronounced sensitiveness to normal human serum of *T. rhodesiense* which has sojourned for some time . . . in vertebrate hosts other than man, provides almost

overwhelming evidence that normal human beings cannot become infected with such strains " [see this *Bulletin*, Vol. 27, p. 804]. Fairbairn writes that in the light of the present experiment both these assumptions appear unfounded.

[In view of the importance of the subject the reviewer may perhaps be pardoned if he makes a few observations on this very interesting paper. In the first place it should be pointed out that by means of omissions Fairbairn has misquoted the reviewer and his colleagues to a very material degree. In the first quotation the words " even though the serum or plasma is diluted to such an extent that its concentration in the medium is only 1 : 25,000 " are omitted, and in the second " how long we do not yet know, but probably it will be found to be comparatively short."

There is of course very great difference between the sensitiveness of a strain which is killed *in vitro* by human serum diluted to the extent of 1 : 25,000 and that which is merely destroyed by undiluted serum ; and in the paper referred to the reviewer and his colleagues were careful on this ground to distinguish between their old laboratory strain of *T. rhodesiense*, which has been in laboratory animals for many years, and their recent " Sherifuri " strain which had been isolated from man for less than one year. We stated that it seemed to us incredible that our *T. rhodesiense* strain which was killed *in vitro* by human serum diluted 25,000 times could infect man, and we were careful to refrain from expressing any opinion regarding the infectibility of the much more recently isolated " Sherifuri " strain, which was much less sensitive to human serum *in vitro*.

It is true that we did not subinoculate rats with the serum-trypanosome mixture at the end of 24 hours—as did Fairbairn, but owing to the extent to which human serum could be diluted and still cause the apparent destruction of all the trypanosomes in the medium within a few hours as judged by microscopic examination, such a procedure did not appear necessary. Assuming, however, that Fairbairn's technique was beyond criticism and that owing to thorough mixing all the trypanosomes were in contact with the undiluted human serum for 24 hours, then the fact that such mixtures were sometimes still capable of infecting rats shows conclusively that the strain was not very sensitive to human serum. The reviewer and his colleagues have pointed out several times that all the individuals in a trypanosome suspension are not killed by the same concentration of serum or drug in exactly the same time ; isolated individuals can sometimes be seen moving actively and apparently in a normal state some time after the vast majority have completely disintegrated.

In short it seems to the reviewer that Fairbairn's results can be explained on the assumption that his strain was barely sensitive to human serum. Undiluted serum destroyed the majority of the individuals, but a few survived, as is shown firstly by the fact that one of the rats inoculated with the 24-hour old serum-trypanosome mixture from the rat of the 19th passage (*i.e.*, the passage from which the human being was injected) became infected ; and secondly by the fact that one of two rats inoculated from the 24-hour old serum-trypanosome mixture of the 21st passage also became infected. As a matter of interest it should be noted that the data set out in Fairbairn's table do not give the slightest evidence that the trypanosomes of the 19th or 21st rat passages were any more sensitive to human serum than were those of the 1st or 2nd passages. For such reasons as these the

reviewer remains unconvinced that " the trypanolytic power of serum, or the lack of it, is no indication of the power of the body to deal with trypanosomes."] *W. Yorke.*

FAIRBAIRN (H.). **The Action of Human Serum *in Vitro* on Sixty-Four Recently Isolated Strains of *T. rhodesiense*.**—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 185–205.

The author has examined the action of human serum *in vitro* on sixty-four strains of *T. rhodesiense* obtained during an outbreak of sleeping sickness in the Kibondo District of Tanganyika Territory.

He employed the technique devised by the reviewer and his colleagues (1929). The temperature was maintained at 37°C. for the 12 hours during the daytime, but, as the incubator had no regulating mechanism, the lamp had to be removed for the night and the temperature gradually fell to about 21°C. Rats were usually sub-inoculated with the trypanosome-serum mixture at the end of 24 hours to ascertain whether the absence of trypanosomes, as shown by microscopic examination, really meant that all the trypanosomes had been killed by the serum. The results of the examination of 64 strains of *T. rhodesiense*, all tested in the first rat passage from man, are shown in a table, the results of which indicate that the majority of the strains tested were resistant to human serum.

The author then passed to a consideration of the question whether the passage of the strains through series of rats had any effect on the resistance to human serum. Seventeen of the 64 strains were consequently repeatedly subinoculated into rats, and their resistance to human serum examined at each rat passage. The results obtained are summarized in a table, which shows that frequently the resistance of the trypanosomes to human serum disappears as early as the second rat passage and may reappear in subsequent passages.

A few experiments with *T. brucei*, made with the first rat passage after isolation, showed that the trypanosome is susceptible to human serum. It is hoped to continue this line of work. The author believes that if it can be shown conclusively that *T. rhodesiense* maintains its resistance to human serum after each cyclical passage through the tsetse, then a biological method of differentiating *T. brucei* and *T. rhodesiense* would result ; those polymorphic trypanosomes, recovered from game or fly, which showed, when tested *in vitro*, at the first rat passage, a resistance to human serum, would be justifiably called *T. rhodesiense*.

The last section of the work relates to the examination of the trypanocidal action of sera obtained from various Kibondo natives who came to the out-patient department for the treatment of yaws, ulcers, etc. In all, 21 sera were examined without any marked variation in trypanocidal action being observed. On two occasions serum was taken from a new sleeping sickness case before treatment, and its trypanocidal power tested against a heterologous strain. On both occasions, they showed similar trypanocidal power to that of Fairbairn's own serum.

The following summary is given :—

" 1. During a recent outbreak of sleeping sickness in the Kibondo District of Tanganyika Territory, the action of human serum was tested *in vitro* at 37°C. against 64 strains of *T. rhodesiense* (all in the first rat passage). The majority of these strains were shown to be resistant.

" 2. It was shown that the resistance to human serum was a very variable quality, fluctuating from rat passage to rat passage.

" 3. In a large number of the 2nd rat passages tested, this resistance to human serum has disappeared, to reappear later; and it is therefore suggested that in future, when testing any strain, it should always be done in the 1st rat passage, or else over a long and consecutive series of subsequent passages.

" 4. Following Yorke, Adams and Murgatroyd's technique, it has been shown that it is not justifiable to say a strain is non-effective [*sic*] just because no trypanosomes are visible in the fluid after 2 to 4 hours, but that this must be established by sub-inoculating rats.

" 5. On the other hand, even though an occasional trypanosome is seen in the fluid at the end of 24 hours, the sub-inoculated rat may not be infected.

" 6. Twenty-nine human sera (both European and native) were tested for their trypanocidal power, and they were all of the same value."

W. Y.

Adams (A. R. D.). **A Record of an Investigation into the Action of Sera on the Trypanosomes Pathogenic to Man.**—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 309–326.

This paper gives details of a considerable number of experiments devised with the object of ascertaining the action of human sera *in vitro* on various strains of trypanosomes—*T. gambiense*, *T. rhodesiense* and *T. brucei*. The technique adopted was that described by Yorke, Adams and Murgatroyd, 1929, except that the strains were usually maintained in guineapigs instead of in mice.

Four strains of *T. gambiense* from Uganda preserved their complete resistance to human serum over a period of 12 months maintenance in laboratory animals. The results confirm the observations of Yorke, Adams and Murgatroyd that human serum fastness is a characteristic of *T. gambiense* and is preserved for a considerable period of time through repeated passages in laboratory animals. In addition one of the strains was tested against the serum from an untreated case of *T. gambiense* infection, from a baboon which had been proved experimentally to be immune to *T. gambiense* infection, from a sheep infected many months with several strains of *T. gambiense*, and finally from a fowl. The serum of the normal human being had no effect on the trypanosomes; that from the sleeping sickness patient destroyed all the trypanosomes when diluted 1 : 2; that from the baboon destroyed all the parasites when undiluted and almost all when diluted 1 : 10; that from the infected sheep destroyed all the parasites when diluted 1 : 10 and almost all when diluted 1 : 50; and that from the fowl had no effect on the trypanosomes. Adams considers that these observations—particularly the failure to demonstrate a powerful trypanocidal substance in the serum of the baboon—are of great interest " in view of their obvious inconsistency with any thesis that trypanocidal body in the serum is alone responsible for immunity against trypanosomal infection."

Four strains of *T. rhodesiense* recently isolated from man were obtained from Dr. Corson of Tanganyika. Each of these strains in the first passage animal showed definite resistance to the action of pure human serum. The results are shown in a table from which it is seen that in the presence of human serum the number of trypanosomes exhibits a marked early decrease and after this immediate drop the decrease during the subsequent 18 hours was very slight. Adams

writes " It would appear that a certain proportion of the parasites is susceptible to the action of human serum and is killed in a short time, whilst the resistant parasites survive the full period of 24 hours at 37°C." [This observation is in harmony with those of FAIRBAIRN who found that although microscopic examination of the serum-trypanosome mixture was negative, nevertheless sometimes inoculation into rats produced infection.]

The four strains were maintained by passage through guineapigs and the sensitiveness to human serum examined from time to time; all four became definitely serum sensitive; Strain A at the 6th passage, Strain B at the 5th, Strain C at the 8th and Strain D at the 3rd passage, in periods varying from 2 to 5 months after isolation from man.

In August 1931, six further strains of *T. rhodesiense* were obtained from Dr. CORSON; all were some months old and had been passed through a number of animals. The results of testing these strains are set out in a table and show that they were all rapidly killed on exposure to strong concentrations of serum. It is noted that these strains had lost their serum resistance more quickly than the previous four strains, and it is suggested that this is possibly due to the fact that the second batch were passaged through rats instead of through guineapigs.

The old Liverpool strain of *T. rhodesiense*, sent to ADAMS by the reviewer, was tested at the same time and was found to be killed by the same great dilutions of human serum as had been shown in earlier work. This strain was found to be rapidly fatal to a sheep and attempts made to infect *G. palpalis* (624 flies were used) failed.

Experiments were next undertaken to ascertain whether " fly " transmission of a strain of *T. rhodesiense* had any effect on its reaction to human serum. Three strains were transmitted by fly from guineapig to guineapig on one or two occasions, and their reactions to human serum noted before and after the passages. The results of these experiments are also summarized in a table from which it is seen that after a single fly transmission loss of resistance to human serum had taken place and that this was not the case when the strain was passaged by the syringe.

The reactions of two strains of *T. brucei* to human serum *in vitro* were studied: the first of these, called the N'songezi strain, was obtained by the author in the Ankole District where human trypanosomiasis is unknown; and the second, Hornby's virulent strain, came from Tanganyika. Both were definitely sensitive to human serum, but not more so than were the *rhodesiense* strains after a few months' passage in laboratory animals. *W. Y.*

DUKE (H. Lyndhurst). **A Study of the Behaviour of *T. rhodesiense* Recently Isolated from Man, in Antelope and Other African Game Animals. Part I.**—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 215–236.

The main object of the research, of which this paper records the preliminary stages, is to ascertain whether, after a year or two in antelope, *T. rhodesiense* stills retains its power of infecting man.

The paper opens with a summary of the discussion which has gone on during the last 20 years regarding the relationship of *T. gambiense*, *T. brucei*, and *T. rhodesiense*. It is now known that *T. rhodesiense* can be introduced into game animals, and clearly this must also happen in nature. The present paper gives details of a number of experiments devised with the object of ascertaining whether certain

game animals could be infected with *T. rhodesiense*, and if so what was the nature of the infection which resulted.

Three strains of *T. rhodesiense* recently isolated from natives of Tanganyika were obtained from Dr. FAIRBAIRN. These three strains (viz. Tinde 1, 2, and 3) were found to be indistinguishable from one another, except in one respect ; whilst Tinde 2 and 3 are characterized by producing very heavy gland infections in Glossina, in the mature gland infection with Tinde 1 the trypanosomes are always much less numerous, and are sometimes so scanty that very careful search is necessary to find them. As this proved to be a constant phenomenon, it seems that this sparse type of gland infection is actually a character of Tinde 1.

A reedbuck, a ntalaganya (*Cephalophus caeruleus melanorrheus*), 3 bushbuck, 1 oribi, 3 wild pigs, 1 pig of an undetermined species, and a serval cat were all infected with one or other of these three strains. In every instance the infection was caused by the bite of cyclically infected tsetse (*G. palpalis* or *G. morsitans*). These experiments are recorded in very considerable detail. It is noted that whilst the reedbuck, bushbuck and oribi showed no signs of trypanosomal infection, the ntalaganya died of uncomplicated trypanosomiasis in 110 days.

Attempts were made to infect Glossina from the antelope after they had been infected for considerable periods, and fly were infected from the reedbuck on the 107th day, from the bushbuck on the 108th day, and from the ntalaganya on the 87th day. The wild pig (*Potamochoerus choeropotamus*) proved to be very susceptible to infection with *T. rhodesiense*, and another undetermined species of wild pig behaved in a similar manner. The serval cat was likewise very susceptible and died on the 45th day of the disease. Tsetse were readily infected from this animal. *W. Y.*

DUKE (H. Lyndhurst). **Relative Susceptibility of the Sexes of Glossina to Infection with Trypanosomes.**—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 355–356.

In this note Duke qualifies the statement made in a previous paper [this *Bulletin*, Vol. 27, p. 847], viz., that there was no significant difference between the two sexes of *G. palpalis* in their susceptibility to *T. gambiense* and *T. rhodesiense*.

Mr. MCDONALD, the Laboratory Assistant to the Human Trypanosomiasis Institute, has recently re-examined the registers wherein are recorded the transmission experiments with tsetse and various polymorphic trypanosomes performed during the last six or seven years, and has reached the conclusion that under laboratory conditions the female of *G. palpalis* is more susceptible to infection with *T. gambiense* or *T. rhodesiense* than is the male. Duke considers that the facts that the female flies feed more readily than the males, and that they tend to survive better in captivity, may have a bearing on this conclusion. *W. Y.*

DUKE (H. Lyndhurst). **The Trypanosomes of Man : their Resistance to Arsenical Drugs.**—*Lancet.* 1933. Sept. 2. pp. 553–557.

This paper appears to have been instigated by recent articles of the reviewer and his colleagues in which they claim to have produced " unequivocal evidence that the acquired character of ' arsenic resistance ' in trypanosomes is transmitted unimpaired through the biological cycle of the parasite in Glossina, its natural invertebrate host."

[*ante*, p. 448]. The main argument, which Duke elaborates with considerable ingenuity in his present very interesting communication, is that it is not safe to reason by analogy, and that it by no means follows because an acquired arsenic-resistance in *T. rhodesiense* is transmitted unimpaired through Glossina the same thing will happen in the case of *T. gambiense*.

The first portion of Duke's paper is devoted to replying to certain criticisms made by the reviewer in respect of an earlier paper by Duke recording experiments performed with the object of ascertaining whether acquired arsenic resistance in *T. gambiense* was transmitted through *Glossina palpalis*. [Nothing seems to be gained by discussing this matter further here; anyone interested can consult the original articles and form his own opinion. Even this, however, seems hardly worth while, as Duke now writes of his earlier work, "that these experiments were not regarded as conclusive is, however, made quite clear in the text of the report." Moreover, it is also quite clear that if Duke now regarded his earlier experiments as conclusive, he could not have written the present paper.]

Duke next passes to a consideration of the fact that different strains in nature exhibit different sensitivity to arsenicals. "From the standpoint of the clinician confronted by native populations affected with trypanosomiasis, normal *T. rhodesiense* is resistant and normal *T. gambiense* is sensitive to therapeutic doses of approved arsenical drugs."

Wallace (1930) found that some of his guineapigs infected with *T. gambiense* were sterilized by a single dose of atoxyl as low as 0·01 gm. per kilo. and none relapsed after 0·03 gm. per kilo.; in guineapigs infected with *T. rhodesiense* doses of 0·03 gm. per kilo. were given without causing any disappearance of trypanosomes and relapse occurred after 0·07 gm. per kilo. Recent work has, however, shown that these conclusions require some modification; they were based upon experiments with a limited number of animals and strains, and it is also highly probable that importance attaches to the age of the infection in the guineapig at the time of the administration of the drug. [The number of parasites in the peripheral blood certainly influences the result in determining the minimum effective dose.] At the present stage of Wallace's investigations, it appears that in guineapigs infected with *T. rhodesiense*, *T. brucei* or *T. gambiense*, an initial dose of 0·03 gm. per kilo. of atoxyl is the critical dose: if trypanosomes fail to disappear from the blood within a week after the administration of this dose to a guineapig during the first two or three weeks of infection, suspicion at once arises that the strain is not normal *T. gambiense*, but either *T. rhodesiense*, *T. brucei* or a *T. gambiense* possessed of abnormal resistance to arsenic. Reference is made to Sherifuri strain from Northern Nigeria, which resembled *T. rhodesiense* in many respects and was found by the reviewer to be completely resistant to aromatic arsenicals; and also to the fact that three of ten Nigerian strains examined by Lester showed a natural resistance to tryparsamide in small laboratory animals.

The practical incentive to research in drug resistance has nothing to do with *T. rhodesiense*. The expression "drug-fastness" used in connexion with human trypanosomiasis means to the medical man the fastness or resistance occasionally exhibited by *T. gambiense* against drugs that normally destroy it. As the reviewer has already pointed out, the matter is of particular importance in the French Congo in view of the prophylactic measures adopted by the French of wholesale

atoxylization. Duke asks himself, what are the possible explanations of the continued presence of trypanosomes in the blood of a *gambiense* case after a full course of arsenic ? He writes " First, he may have been reinfected. This cause can be ruled out at once in some cases. Secondly, his system may have been unable to cope with the drug owing to some temporary or constitutional disability. Thirdly, he may be infected with a strain possessing an abnormally high natural resistance to arsenic. And finally, if his trypanosomes have indeed acquired increased resistance by contact with the drug, there is always a probability that the strain was originally possessed of an abnormal natural resistance." Regarding the second possibility Duke refers to the work of the reviewer and his colleagues, who showed that a strain resistant in one species of host is likewise resistant in another, and furthermore that the quality of resistance is inherent in the trypanosomes themselves. Duke considers, however, that it does not necessarily follow that it will manifest that resistance equally when trammelled by the reactions of a host animal capable, even when unaided by a drug, of exerting a restraining effect on the trypanosomes' activities. In support of this he quotes the enormous differences noted by the reviewer in the response of one and the same strain to tryparsamide in different species of animal. [In the reviewer's opinion these differences are largely if not entirely due to variations in the rate of reduction and excretion of the drug.]

With regard to the third possible explanation Duke states that 4 years ago he requested medical officers in Uganda to collect and send him any cases that had resisted treatment with tryparsamide in the West Nile area. Three such were received ; the first was an undoubted case of *T. rhodesiense*, but the other two were *T. gambiense*. When examined in the guineapig both the last strains proved slightly more resistant than those previously tested. One of the strains was non-transmissible, but the other was readily transmitted by *G. palpalis* and its reactions to arsenic then were found to be as before transmission. [This seems to ignore the possibility that the arsenic given in the West Nile area to these patients before they were sent to Duke had something to do with the enhanced arsenic resistance found by Duke.]

The only records of attempts to make recently isolated strains of *T. gambiense* resistant to drugs are those of Wallace at Entebbe and of Taylor in West Africa, who both succeeded after some trouble in preparing a drug-fast strain. Neither, however, was able to transmit the fast strain through Glossina. Duke considers that it is not unlikely that the majority of so-called drug-fast strains of *T. gambiense* in man in Africa are merely strains possessed of an exceptional natural resistance to arsenic, and that such strains will no doubt retain their resistance when passed through the tsetse. He is not convinced that the reviewer and his colleagues are justified in regarding the conclusions drawn from their study of *T. rhodesiense*, *T. brucei*, *Glossina morsitans* [and *G. palpalis*] as applicable to the sphere of *T. gambiense* and its normal vectors *G. palpalis* and *G. tachinoides*.

Duke summarizes his points as follows :—

" The exemplary series of investigations carried out in the last few years by Yorke and his colleagues have revolutionised our conceptions of drug resistance in trypanosomiasis. As the result of these researches we now know how to maintain trypanosomes alive in vitro for a considerable period of time ; we know the manner in which arsenical drugs act on the trypanosomes ; how best to increase the natural resistance of a strain, and

how that resistance operates; and that the resistance acquired is not resistance to arsenic but to the phenyl radicle present in all trypanocidal arsenical drugs used in treatment of the disease in man; and, finally, that a strain resistant in one species of host is resistant in another. But the final word has not yet been spoken on the subject of acquired resistance in normal *T. gambiense* against tryparsamide and its allies. The outstanding questions seem to me to be :—

" (1) Can a strain of *T. gambiense* recently isolated from a patient into whose blood the trypanosome was introduced by biologically infected tsetse, acquire permanent resistance to a drug as the result of exposure to occasional small doses ?

" (2) If it can do so, does the acquisition of resistance in any way impair the transmissibility of the strain by tsetse ?

" (3) If the strain retains its transmissibility by tsetse, does the acquired resistance to arsenical drugs survive passage through the fly ?

" The question whether acquired drug resistance survives the passage of a strain through tsetse is but one aspect of an important biological problem —namely, the rôle of the insect intermediary in maintaining the character of the protozoon it transmits.

" If Yorke and his colleagues' interpretation of their results is correct, then we must conclude that an acquired character can survive the seemingly drastic changes that a trypanosome undergoes during its cyclical development in the tsetse. Schilling, as the result of transmission experiments performed with a highly virulent strain of *T. brucei* and *G. morsitans*, has lately reached diametrically opposite conclusions, maintaining that passage through the tsetse purges a strain of all acquired abnormalities.

" The subject is thus of great biological as well as practical interest and calls for the most exhaustive inquiry along several different lines of research."

[The recent paper of VAN HOOF and HENRARD summarized in the present number bears directly on this subject and may perhaps resolve some at least of Duke's doubts.] *W. Y.*

VAN HOOF (L.) & HENRARD (C.). La transmission cyclique de races résistantes de " Trypanosoma gambiense " par " Glossina palpalis." [**Cyclical Transmission of Resistant Strains of** *T. gambiense* **by** *G. palpalis.*]—*Ann. Soc. Belge de Méd. Trop.* 1933. June 30. Vol. 13. No. 2. pp. 219–244.

The main object of the work described in this paper was to ascertain whether an arsenic-resistant strain of *T. gambiense* could be transmitted by Glossina and, if so, whether the strain, after cyclical passage through the tsetse preserved its resistant character.

Details are given regarding 8 strains of *T. gambiense* used in these experiments but, as successful transmission was only accomplished in respect of two of them, it will suffice to mention only these two.

Strain G, Bernard Lisala.—This patient, aged 30, was probably infected on the river n'Giri near Kinwenza. The disease was diagnosed on 19 Sept., 1932, by gland puncture; at this time lumbar puncture showed 80 cells per cmm. Between 22 Sept. and 23 Nov., 1932, he was given 9 injections each of 2 gm. of tryponarsyl; lumbar puncture now showed 20 cells per cmm. On 14 Dec., 1932, many trypanosomes were found. The patient was then treated with Dn 12 [a pentavalent antimonial compound of quinoline] to which the trypanosome showed no resistance. [From data supplied in the tables, it appears that Glossina were fed on this patient between 15 Dec. and 26 Dec., 1932.]

Strain H, Momfo Essa.—A woman, aged 25, infected at Black River (Chenal) and diagnosed by gland puncture on 22 Aug., 1932; at this date the spinal fluid contained 48 cells per cmm. From 22 Aug. to 1 Dec.,

1932, the patient was given 15 injections each of 2 gm. of tryponarsyl at irregular intervals. The trypanosomes did not disappear from the circulation. On 16 Dec., 1932, the blood contained parasites, and the spinal fluid 21 cells per cmm., and albumen 0·4. The trypanosome was equally resistant to Dn 12, a single dose of 0·25 gm. failing to sterilize the blood. From 7 Jan. to 25 Jan., 1933, she was given 6 injections each of 0·5 gm. of Dn. 12, and on 30 Jan. trypanosomes were numerous in the blood. [The table shows that flies were fed on this patient between 24 Dec., 1932, and 4 Jan., 1933.]

Details of all the transmission experiments performed on these 8 strains, and on two others, Kunku and Sanzala, concerning which no information is given, are set forth in a table, and the main facts summarized in a shorter table which is reproduced below.

It will be seen from this table that the only successful transmission experiments were those made with the last two strains. The number of flies used in the first two experiments is small, but the authors state that when the results are compared with those obtained with the last two strains, the former seem to be entirely non-transmissible. The next six attempts at transmission were made by feeding flies not on the patient, but on animals either inoculated directly from the patient or at least of an early passage. In none of these instances did the authors succeed in obtaining a biologically infected Glossina, although in some cases quite a number of gut infections were obtained (*vide* Table, Strains Boeke and Tassi Kikela). The authors discuss this interesting point at length; they consider their findings support DUKE's contentions that certain strains are non-transmissible. They furthermore draw the important conclusion that a single mechanical passage (by means of the syringe) of a trypanosome from a patient to a guineapig may suffice to render the trypanosome, whether it be arsenic resistant or not, completely non-transmissible. [There is, of course, no proof that it was the transference of the strains to guineapigs which produced this result.]

Interesting details are given of the tests made on the two strains which were transmitted; these were as follows :—

Strain G, Bernard Lisala.—A monkey infected by the bites of the Glossina which had been previously infected from the patient showed trypanosomes in its blood for the first time on 24 Jan., 1933. On 27 Jan. it was given 7 cgm. per kilo of tryponarsyl: trypanosomes disappeared. A guineapig which also became infected on 24 Jan. was given on 27 Jan. rather more than 10 cgm. of tryponarsyl per kilo: trypanosomes disappeared. Another guineapig which became infected on 1 Feb. received on 9 Feb. 7 cgm. per kilo of tryponarsyl and failed to become negative within 48 hours.

From these data the authors conclude that the resistance of this strain after transmission was approximately 7 cgm. of tryponarsyl per kilo., which they state represents 3·5 to 4·0 gm. for a medium sized negro. [? A warrantable assumption.] It is considered that this strain was by way of becoming resistant before and after transmission.

Strain H, Momfo Essa.—A guineapig, which became infected on 27 Jan. was given on 9 Feb. 15 cgm. of tryponarsyl per kilo.; its blood did not become negative until 12 Feb. Another guineapig which also became infected on 27 Jan. was given the same day 10 cgm. of tryponarsyl per kilo.; the blood remained positive until 7 Feb. when it was given a dose of 25 cgm. per kilo without the blood becoming negative.

Source of strain. *T. gambiense.*	Date of experiments.	Total number of flies dissected.	Total number of flies infected.	Percentage of infections.	Number of infected flies alive on the 15th day.		Index of transmissibility.
					With glands infected	Total	
Kunku ...	29.12.31 to 29.2.32	36	0	0	0	0	0
Sanzala ...	29.12.31 to 12.2.32	45	0	0	0	0	0
Cobaye Tshéla	15.1.32 to 16.8.32	301	2	0·66	0	0	0
Singe 4 Tshéla	16.6.32 to. 16.8.32	98	0	0	0	0	0
Cobaye Goma	9.8.32 to 6.10.32	95	0	0	0	0	0
Cobaye Ikongo Vivina	14.8.32 to 22.10.32	46	1	2·18	0	0	0
Cobaye Boeke	7.11.32 to. 19.1.33	110	27	24·53	0	16	0
Cobaye Tassi Kikela	29.11.32 to 19.1.33	161	35	21·7	0	12	0
Lisala Bernard	15.12.32 to 31.1.33	169	17	10	5	8	6·28
Momfo ... Essa	24.12.32 to 8.2.33	*160	23	14·3	6	16	5·4
		†160	14	8·7	6	7	7·5

* Index calculated after taking account of all late infections communicated at the end of the experiment by the animal serving to maintain the flies (guineapig) and to which the infections had been transmitted.

† Index calculated after eliminating this source of error.

From these experiments the authors conclude that tryponarsyl-resistance in *T. gambiense* is preserved after cyclical passage through *Glossina palpalis*. [It is unfortunate that the authors' evidence was not a little more precise. It would have simplified matters had they infected guineapigs from these patients, Bernard Lisala and Momfo Essa, before the transmission experiments and ascertained

precisely the degree of resistance of the strains in these animals at this time. They could then have compared with these the data they obtained with the guineapigs infected by the cyclically infected Glossina, and by this means have decided beyond all doubt whether the strains had changed as the result of passage through the fly. There seems, however, no reasonable ground for doubting that the transmitted strains—particularly the second—were definitely resistant, and that the authors have in fact succeeded in demonstrating that tryponarsyl-resistance in *T. gambiense* is transmitted through *Glossina palpalis*. This work confirms that of the reviewer and his colleagues, which presumably the authors have not seen, as they do not refer to it ; this *Bulletin*, Vol. 30, p. 448]. *W. Y.*

BARLOVATZ (A.). Une démonstration statistique de la transmissibilité à l'homme de trypanosomiase résistante au tryponarsyl. [**Transmissibility to Man of Trypanosomes Resistant to Tryponarsyl.**]—*Bull. Soc. Path. Exot.* 1933. Apr. 5. Vol. 26. No. 4. pp. 623–632.

After a preliminary discussion of certain recent literature relating to the subject of arsenic-resistance, details are given of 9 cases in the Tobi-Lushiko sector of the Belgian Congo, which were found to have arsenic resistant infections at the time of treatment in 1932

At the commencement of his paper Barlovatz states that the work of the reviewer and his colleagues has shown that resistance of trypanosomes to tryparsamide implies resistance to other pentavalent arsenicals, but not to trivalent arsenicals such as novarsenobillon ; Barlovatz, however, found that his patients were also resistant to novarsenobillon. [Barlovatz has misunderstood the reviewer and his colleagues, who clearly showed that resistance to any of the aromatic compounds of arsenic or antimony implies resistance to all the others—pentavalent, trivalent or arsenobenzol compounds.]

The results obtained by the reviewer in the production of resistant strains of trypanosomes by exposure of the parasites to various concentrations of arsenicals *in vitro* appear to explain the high degree of resistance exhibited by certain patients seen by Barlovatz at Mayumbe, where, since 1922, the standard courses of both atoxyl and tryparsamide have been very large. Barlovatz showed by injection of guineapigs that these patients were resistant to treatment because they were infected with resistant parasites.

Six of the nine cases of which details are given and on which most of the author's argument is based were from the village of Shakasumbi in the Tobi-Lushiko sector. This sector had previously been visited only once in 1929 by two native sanitary agents, who administered to the sick a standard course of 24 gm. of tryparsamide. As there is neither mission nor hospital in the district, there has been a minimum of medical intervention.

Details of the first case, which can serve fairly well as a type of the lot, and which probably infected the others, are as follows :—

Muenze ♀, 30 yrs. Treated in 1929 by sanitary agent with 10 doses each of 2 gm. tryponarsyl, becausc she was a suspected case of sleeping sickness (puncture negative). On 21.8.32 : gland puncture + ; lumbar puncture 3·2 lymphocytes, albumen normal ; given on 21.8.32 tryponarsyl 1 gm., 30.8.32 tryponarsyl 1·8 gm. and 31.8.32 tartar emetic 6 cgm. Lost to sight (as were also the other cases, during the author's absence) up to 8.10.32, when she was given a regular course of 2 gm. doses of tryponarsyl

per week up to a total of 15 gm. The course finished on 27.11.32, and on Dec. 2nd the blood was found to be positive by the triple centrifugation method ; glands negative. Moranyl was then given.

Shakasumbi contained 24 inhabitants (10 men, 9 women, and 5 children). When examined on Aug. 1932, there were found :—5 old cases treated in 1929, of which one (Case 1) had trypanosomes in the glands in 1932 ; 4 new cases (Cases 3–6) with positive glands and two new cases recognized by lumbar puncture (Case 2 and another, who responded well to tryponarsyl). Except for the last case all the patients of this group were resistant to tryponarsyl—a coincidence which could hardly be attributed to pure chance.

The author draws particular attention to the fact that in all these cases treatment was suspended for 31 days (owing to his absence) after the first three injections of tryponarsyl had been given. He inquires whether this fact had anything to do with the failure to cure by the subsequent doses, and as the result of certain considerations, which are stated in detail, he concluded that it had not. He observes that three of the most typical cases were resistant before the interruption of the treatment. Experience has shown that in the treatment of native cases a positive gland puncture, after 2 injections of tryponarsyl, is not found more than once in 35 cases, and that probably this figure is too high. Three of 4 cases of Shakasumbi were positive after 2 injections.

Attention is drawn to the interesting fact that in 7 of these 9 resistant cases the cerebrospinal fluid was normal. *W. Y.*

Schwetz (J.). Sur un cas de trypanosomiase (humaine) arsénico-résistante. [**Case of Arsenic Resistant Trypanosomiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. June 30. Vol. 13. No. 2. pp. 211–213.

An account is given of a case of sleeping sickness which proved resistant to tryparsamide, but which was subsequently cured by Fouadin (antimosan).

The patient was a woman, 25 years of age, who was recognized as infected at Thysville (Stanleyville District) on 5 October, 1931. She was given a course of treatment consisting of 12 weekly injections, each of 5 gm. of tryponarsyl ; on 31 Dec. a gland puncture was positive. The treatment was then repeated and up to 16 April, 1932, she had received another 32 gm. of tryponarsyl. On 19 April, lumbar puncture showed the spinal fluid to be practically normal (lymphocytes 3·2, albumen 0·18). She was then repatriated to Stanleyville and treatment continued ; from 24 May to 30 July, 1932, 9 further injections of tryponarsyl were given.

On 22 August she was sent to the laboratory for examination. Numerous large cervical glands were found, and on puncture of one of them trypanosomes were found to be numerous ; the blood was negative. Lumbar puncture showed the spinal fluid contained 1·2 lymphocytes per cmm. The general condition was excellent.

On 24 August the patient was given a course of antimosan. The first dose was 1·5 cc., the second 3·0 cc., and the remaining doses 5·0 cc. By 12 Sept. she had received 45·0 cc. The glands became negative in a few days and the patient was apparently cured by the course.

Rodhain in commenting on this case compared it with certain cases recorded by Barlovatz, in which apparent arsenic-resistance was associated with normal cerebrospinal fluid. It seemed to him that

although in these cases tryparsamide was unable to sterilize the infection, it had nevertheless succeeded in preventing the invasion of the central nervous system. *W. Y.*

HOARE (C. A.) & COUTELEN (F.). Essai de classification des trypanosomes des mammifères et de l'homme basée sur leurs caractères morphologiques et biologiques. [**Classification of Trypanosomes of Mammals and Man.**]—*Ann. Parasit. Humaine et Comparée.* 1933. May 1. Vol. 11. No. 3. pp. 196–200. With 1 folding table.

The essential portion of this paper consists of a useful table, which not only classifies the trypanosomes of mammals, but summarizes all their main characters, *e.g.*, the chief morphological characters, their vertebrate and invertebrate hosts, their geographical distribution, and their pathogenicity for laboratory animals.

The genus is divided into two main groups having the following characters :—

Group A.—Blepharoplast non-terminal ; posterior extremity effilated and pointed ; usually of large size ; in the intermediate host the infectious stages are found in the posterior intestine, and transmission is by contamination with the faeces ; the trypanosomes are of little or no pathogenicity and are easily cultivated. This group is called by the authors the *lewisi* group, and contains in addition to this trypanosome, *T. theileri*, *T. melophagium*, *T. theodori*, and *T. cruzi*.

Group B.—Blepharoplast terminal or sub-terminal. In the invertebrate host the infectious forms are found in the proboscis or salivary glands, except in the *T. evansi* sub-group, where there is no cyclical evolution ; transmission is by inoculation, except in the case of *T. equiperdum*, where the infection is spread by coitus ; the trypanosomes are pathogenic and can only be cultivated with difficulty if at all. This group is divided into two divisions, according to whether the trypanosomes are monomorphic or polymorphic ; the latter division consists of the *brucei* group in which in the invertebrate host the infective forms are found in the salivary glands. It contains *T. brucei*, *T. rhodesiense* and *T. gambiense*. The monomorphic division is divided into two subdivisions, according to whether the flagellum is free or not free. The latter subdivision consists of the *congolense* group in which the infected forms are found in the proboscis of the invertebrate host ; this subdivision consists of *T. congolense* and *T. simiae*. The subdivision with a free flagellum is again subdivided into a group with a pointed posterior extremity, in which there is no development in the intermediary host and transmission is mechanical or by contact. This is called the *evansi* group and consists of *T. evansi*, *T. equinum*, and *T. equiperdum*. In the second group the posterior extremity is rounded and development in the intermediate host is limited to the proboscis. This consists of *T. vivax*, *T. caprae*, and *T. uniforme*. *W. Y.*

BRAZZAVILLE. Rapport sur le fonctionnement de l'Institut Pasteur de Brazzaville pendant l'année 1931. [**The Work of the Brazzaville Pasteur Institute in 1931.**]—105 pp. 1932. Brazzaville : Gouvernement Général de l'Afrique Équatoriale Française.

This notice deals only with human trypanosomiasis.

In the year under review of 69,108 natives examined for trypanosomiasis 195 were found infected ; 93 of these were discovered on tours

of inspection, 85 because they were ill, 10 had applied for permission to travel by boat, and 7 were discovered because they desired an engagement. In addition to the 195, 763 old cases were treated and 80 suspects. The fatality rate in the year was 2·2 per cent. A table shows the number of Europeans infected yearly for 18 years, 92 in all or an average of 5·1 a year. A second table shows the numbers of natives examined yearly since 1910 and the number of diagnoses of trypanosomiasis: the proportion of infected has fallen steadily from 7·4 to 0·2 per cent. (the number of examinees has risen 17 fold). It is stated that 32 per cent. of persons recognized to be infected at Brazzaville do not show trypanosomes except in the cerebrospinal fluid; they have passed the lymphatic and blood stage before they reach the doctor; consequently routine examinations for trypanosomiasis are rarely positive. Probably such persons would have parasites intermittently in the circulation and would be capable of infecting tsetse. A table shows that whereas between 1914 and 1924 when treatment was by atoxyl, tartar emetic, and novarsenobenzol, the yearly fatality averaged 36 per cent., in 1925–31 when tryparsamide and Fourneau 270 were used, it averaged 11·5 per cent.; this refers to the treatment centre where only severe cases are admitted. Of all persons infected, as stated above, the fatality was 2·2 per cent. Of the patients treated in 1931, 88 were at the first stage, and 107 at the second. Of the 1st stage treatments 96 per cent. were successful and of the 2nd stage 72 per cent. [but the period of observation is not stated].

Of 758 old cases examined and treated in the course of the year 70 or 9·2 per cent. have relapsed and 17 have died; 14 had a blood relapse and in one there was, in the author's opinion, a genuine arsenic resistance. Blood relapses after tryparsamide treatment were treated by Fourneau 270 and in nearly all blood sterilization was obtained; the author considers this to be the best arsenical trypanocide. 30 had a nervous system relapse, and in 20 of these treatment caused the albuminosis of the C.N.S. to return to normal. In 3 instances reinfection occurred.

The report deals also with the usual activities of the Institute [see this *Bulletin*, Vol. 29, p. 178]. *A. G. B.*

COGHLAN (B. A.). **Notes on One Hundred and Ten Cases of Rhodesian Sleeping Sickness, with Special Reference to Prognosis and Treatment.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. June 29. Vol. 27. No. 1. pp. 67–84. [12 refs.]

Details are given concerning the results of treating two groups of Rhodesian sleeping sickness patients, comprising 110 cases, with a mixed treatment of Bayer and tryparsamide, and the symptoms are studied with a view to prognosis.

Group I (47 cases) were given 5 gm. of Bayer 205 (1 gm. at weekly intervals) followed after 1 month's rest by a course of at least 20 gm. of tryparsamide (3 gm. at weekly intervals). Group 2 (63 cases) were given 3 gm. of Bayer 205 (1 gm. every alternate day) followed after a week's interval by a course of 10 gm. of tryparsamide (3 or 4 gm. at weekly intervals). These two treatments, the author states, are fairly representative of the course given to sleeping sickness patients to-day. The former he designates as "prolonged thorough treatment" and the latter as a "short intensive treatment." The inquiry was primarily undertaken in order to try and gauge the prognostic outlook for sleeping

sickness patients and to ascertain the relative value of various signs in influencing this outlook.

The most common signs of Rhodesian sleeping sickness in their order of frequency are adenitis, oedema, tremor, enlarged spleen, loss of flesh, and pronounced weakness.

The period at which the patient comes to hospital for treatment has, of course, a big influence on the development of the commoner signs ; *e.g.*, oedema, tremor, and enlarged spleen may not have time to develop if treatment is begun early enough, but, as in the present series of cases 4 weeks was the average time which had elapsed from the onset of symptoms, a number of signs were present in the majority of cases. The author takes each of these signs in turn and tries to show its significance in prognosis. The results are summarized in a series of tables. For example, adenitis is first considered, and the patients of each group are classified according to whether or not adenitis was present. In Group I, 36 patients had adenitis at the time of treatment, and 47·1 per cent. were dead in 3 years ; 11 patients of this group did not exhibit enlarged glands, and 72·5 per cent. were dead in 3 years. In Group 2, 58 cases had adenitis, and 51·6 per cent. were dead in three years ; 4 cases did not have enlarged glands, and 100 per cent. were dead in 3 years. These results, in the author's opinion, tend to show that adenitis is a favourable sign. In the same way he deals with oedema, which he considers to be a bad sign, tremor, which is stated to have little significance on prognosis, and enlarged spleen, the significance of which it is difficult to assess on account of malaria in the district. As regards wasting the author writes, " when wasting is present to a noticeable degree, and the patient attends regularly during the prolonged period necessary for Treatment No. 1, the prognosis is not influenced by this sign, but when the patient fails to attend regularly, and as a result only receives partial treatment or Treatment No. 2, then his outlook is definitely adversely influenced and he stands only one chance in six of making a complete recovery." The same is said to be true with regard to weakness.

In two lengthy tables details are given concerning each of the 110 cases treated. From these tables it is seen that of the 47 cases comprising Group I given the " prolonged thorough treatment," 22 were quite fit at the end of the 4th year, and of the 63 cases comprising Group 2, who received the short intensive course, 23 were fit at the end of the 4th year. From this the author concludes that " prolonged thorough treatment " with Bayer and tryparsamide gives better results than " short intensive treatment " with these drugs. The author points out that he believes that if a patient remains well for a period of 3 years after the conclusion of treatment, he seldom, if ever, relapses later. Among the records of 410 cases to which he had access, he could only find one instance in which a patient had relapsed for the first time later than 3 years after the end of treatment.

The author next passes to a consideration of the influence exerted by the condition of the cerebrospinal fluid, and in a table his cases of each group are classified according to whether the number of cells in the cerebrospinal fluid was greater or less than 20 per cmm. In Group I, 24 patients had a cell count greater than 20, and 70·8 per cent. were dead in 3 years ; 13 had a cell count less than 20, and only 22·9 per cent. were dead in 3 years. In Group 2 the corresponding figures are 62·3 per cent. and 33·2 per cent.

As a result of his survey of the data recorded in this paper, the author considers certain signs are of paramount importance when trying to reach a prognosis in any case. These signs in order of importance are :—

1. The condition of the cerebrospinal fluid as ascertained by lumbar puncture.
2. The presence of pronounced, observable weakness.
3. Definite loss of flesh.
4. The presence of oedema.

[It seems to the reviewer, as the result of critical study of Coghlan's tables, that it is doubtful whether some of his conclusions are justifiable in view of the small number of cases which fell into some of his classes.]

W. Y.

Laquieze & Berny. Note sur onze observations de trypanosomés atteints de frigidité génitale. [**Sexual Impotence in Trypanosomiasis : Eleven Cases.**]—*Ann. de Méd. et de Pharm. Colon.* 1933. Jan.–Feb.–Mar. Vol. 31. No. 1. pp. 96–100.

Details are given of eleven cases of trypanosomiasis who exhibited sexual impotence, and on consideration of these cases the authors have drawn certain conclusions. In an endemic area, when a native complains of impotence without any of the usual causes, one should think of trypanosomiasis ; sometimes, even if examination of the blood and gland juice is negative and the cerebrospinal fluid is unchanged, treatment with tryparsamide will give excellent and permanent results. Stress is laid on the fact that a patient suffering from impotence is not necessarily an advanced case of the disease. Three of the eleven cases were in excellent condition and had normal spinal fluids.

Sexual frigidity is, in the author's opinion, a good sign of trypanosomiasis and is apparent in 2 per cent. of cases about 1 to 1½ years after infection. Treatment with tryparsamide gave excellent results.

W. Y.

Laquieze & Berny. Note sur l'arrêt des menstruations chez les trypanosomées. [**Arrest of Menstruation in Trypanosome Infections.**]—*Ann. de Méd. et de Pharm. Colon.* 1933. Jan.–Feb.–Mar. Vol. 31. No. 1. pp. 100–101.

The authors have re-investigated the question of the effect of trypanosomiasis on menstruation. They have examined the point in respect of 140 women (sexually mature and non-pregnant) ; of these 93 were in the first stage of sleeping sickness and 47 in the second stage. Among the first group 84 menstruated regularly, and in 9 (10 per cent.) menstruation had ceased ; in the second group 36 menstruated regularly and in 11 (24 per cent.) it had ceased. Menstruation frequently returned quickly as the result of treatment, usually 2 injections of atoxyl or Fourneau 270 sufficing. *W. Y.*

Chambon. Trypanosomiase humaine observée chez un enfant âgé de cinq jours. [**Trypanosomiasis of a Five-Days-Old Baby.**]—*Bull. Soc. Path. Exot.* 1933. Apr. 5. Vol. 26. No. 4. pp. 607–608.

A child 5 days old was found on 15th October, 1926, to be infected with trypanosomes ; it was born in the village of Mboumo, Cameroons.

The inhabitants of this and neighbouring villages were at that time heavily infected with trypanosomiasis, *e.g.*, Nemayong 69·8 per cent., Mboumo 79·2 per cent., Eko 77·9 per cent. It is noted that the mother was 28 years of age, had been found to be infected on 15 June, 1925, by DE MARQUEISSAC, and that she had been given an injection of 1 gm. of atoxyl and had then disappeared. Reference is made to other cases of infection in very young children. JAMOT recorded a case in a child of 12 days and LE ROUZIC, MONTESTRUC and MONTALIEU discovered three cases in infants aged 10, 12 and 9 days, respectively.

In the discussion which followed this note, CAZANOVE pointed out that FABRE found trypanosomes in the blood of a few days' old child of an infected mother. LEGER cited several somewhat similar cases. KELLERSBERGER agreed with Chambon that in cases like those described, one had to consider the possibility of intra-uterine infection.

W. Y.

LAQUIEZE & BERNY. La parfaite tolérance du noir pour la ponction lombaire et sa réalisation très pratique dans un secteur de prophylaxie en A.E.F. [**Tolerance of the Negro to Lumbar Puncture.**]—*Ann. de Méd. et de Pharm. Colon.* 1933. Jan.–Feb.–Mar. Vol. 31. No. 1. pp. 93–96.

This is a plea for the regular employment of lumbar puncture as a means of diagnosis, and as an aid to treatment, in trypanosomiasis. Between 1st Aug., 1930, and 30th Sept., 1932, no less than 2,715 punctures have been made during sleeping sickness work in Sector 12b Nola (Middle Congo). Although about a third of these were done in the bush not a single accident occurred, and the procedure was well tolerated by the natives and readily accepted by them as a necessary part of their treatment.

W. Y.

BARLOVATZ (A.). Les rachicenthèses capillaires. [**Rachicentesis with a Fine Needle.**]—*Bruxelles-Méd.* 1933. Mar. 26. Vol. 13. No. 21. pp. 583–585.

In this note the author advocates the use of fine needles for lumbar or sub-occipital puncture, mainly on the ground that there is less trauma.

The needles ordinarily used for lumbar puncture are 1 mm. in diameter, *i.e.*, about 0·78 sq. mm. With a needle of 0·6 mm. diameter the figure falls to 0·28 sq. mm., with one of 0·5 mm. to 0·2 sq. mm., and with one of 0·4 mm. (the finest used by the author) to 0·13 sq. mm. The relation of the surface is then 19 : 7 : 5 : 3.

Practically it is impossible to assess the reactions following the use of the different sized needles, but Barlovatz points out that most of his punctures are done on ambulant cases who are not drugged, and who frequently return home, sometimes travelling considerable distances the same day. As a rule the reaction is absolutely nil, but occasionally, even when a needle of 0·5 mm. diameter is used, he has seen violent reactions. Similarly he has never observed any severe symptoms on sub-occipital puncture, most of the patients make no complaint. Hitherto he has made some 10,000 lumbar punctures and more than 4,000 sub-occipital punctures. Among the former he has had no deaths and no untoward symptoms lasting more than a few days. The lumbar

puncture in the bush, provided it is made with a fine needle, is no more dangerous than an intravenous injection.

In his earlier sub-occipital punctures the author used needles of 0·9 mm. in diameter and with a long bevel. With such needles he has had two very severe meningeal haemorrhages, and one immediate fatality in a child. It is noted that puncture of the bulb in animals is frequently immediately fatal When, however, he used a small needle of 0·5 mm. diameter he had no untoward results, even though the nervous centres were punctured. He asks why the nervous tissue is so often punctured and states that the reason is that the directions given in the classical books are quite inexact, at least for the Congo native. The nervous tissues instead of being 5 cm. below the skin in a good puncture are 4 cm. or less, and as a rule in the adult the fluid is obtained when the needle is inserted 3–3·5 cm. With very fine needles it is necessary sometimes to aspirate with a syringe.

Which method is to be preferred, the sub-occipital or the lumbar puncture ? The former is the more easy, and it is not attended by any subjective phenomena, but it has the disadvantage, especially when a large needle is used, that the fluid is often contaminated with blood ; in order to get sufficient pressure the patient must be lying down at the time of sub-occipital puncture, and the process of obtaining the fluid with a fine needle is even then very slow, sometimes 10 mins. is required for 5 cc. of fluid. Lumbar puncture provides the fluid more rapidly and rarely contaminated with blood. Which of the two procedures gives the more significant results is not easy to say. Sometimes the fluid taken at the two levels is identical, but sometimes there are great differences. A discussion of the reasons for this are beyond the scope of this work. *W. Y.*

Ramos (A. Silveira). Tratamento dos estados avançados da doença do sono pelas injecções intra-carotidianas de medicamentos tripanocidas. [**Sleeping Sickness in Advanced Stage treated by Intracarotid Injection of Drugs.**]—Reprinted from *Med. Contemporanea.* 1933. Mar. 5. Vol. 51. No. 10. pp. 63–66.

The author cites cases of sleeping sickness in the later stages in which rapid improvement followed intra-arterial injection of tryparsamide or Bayer 205. Before trying the method on human beings, he experimented with dogs and found that they stood large doses and high concentrations perfectly well—4·8 gm. (10 cc. of a 48 per cent. solution) of tryparsamide in a dog of 12 kgm.

For the first injection given to a man he exposed the carotid under anaesthesia, but not for subsequent injections to this patient nor to any others. The patient lies on his back with head turned a little to the side opposite to that selected for injection ; the site of election is the lower level of the larynx at the anterior border of the sterno-cleido-mastoid. The patient is as a rule too ill to mind the slight manipulation required. The artery is pressed against the larynx, or better the transverse process of a cervical vertebra, and must not be relaxed until the injection is finished, and this should be given very slowly. The doses used were from 1–3·5 gm. Six cases are detailed, one of which may be quoted as an example :—

J. M., male, 42 years, very somnolent, almost comatose ; does not reply to questions ; no desire for food ; enlarged glands in anterior and posterior triangles, knee jerks exaggerated ; incontinence of sphincters. Trypanosomes in c.s.f. ; albumen present in spinal fluid 1 gm. per litre, lymphocytes

160 per cmm. Photophobia, retinal anaemia. Tryparsamide 1 gm. in 3 cc. injected into the right carotid (Oct. 23rd, 1931) without any untoward symptoms. Ophthalmoscopic examination an hour later showed the same conditions. The next day no trypanosomes were seen in the spinal fluid ; there was less photophobia and on 25th Oct. the retina was less anaemic and two days later was " obviously better." On 28th clinical state as before. On 29th 3 gm. tryparsamide in 10 cc. water injected into left carotid. Immediately after, the pupils dilated, the pulse became thin, uncountable, but irregular, with general state of collapse. [This was ascribed to the injection being made too rapidly ; it soon passed off completely.] On 30th the general condition was much better, control of sphincters returned, he began to reply to questions, was able to take food, and could walk, but reeled. The eye condition was better. December 5th " general state excellent," felt well, enjoyed his food and walked normally. C.s.f. albumen 0·56 per litre, lymphocytes 17 per cmm., no trypanosomes seen. December 9th 3 gm. tryparsamide in 10 cc. water injected into right carotid ; bore it well. January 22nd, 1932, vision normal, general state excellent, c.s.f. albumen 0·35, lymphocytes 12 per cmm. Left hospital showing no symptoms.

The author concludes :—

1. After intra-carotid injection of tryparsamide trypanosomes disappear from the blood [they did so in other patients] and the cerebro-spinal fluid ; nervous and mental symptoms disappear and the spinal fluid becomes more normal.

2. The procedure needs no special preparation and can be carried out even in the bush (em plano mato).

3. Injection can be repeated on the same side.

4. No untoward symptoms or ocular lesions resulted ; slight circulatory retinal changes might be seen but without any damage to vision.

5. Though not excluding subcutaneous treatment, in patients in whom a speedy and safe effect on the encephalitic symptoms is called for the intra-carotid route is indicated. *H. H. S.*

Launoy (L.). Nouveaux documents statistiques pour servir à l'étude du mécanisme de l'action trypanocide du 205 Bayer-309 Fourneau. [**Mechanism of Trypanocidal Action of Bayer 205.**]—*C. R. Soc. Biol.* 1933. Vol.. 113. No. 19. pp. 276–279.

This paper records further observations made with the object of throwing light on the mechanism of the trypanocidal action of " Bayer 205 " [*ante*, pp. 114 ; 445].

A series of mice were inoculated at intervals from 2 to 24 hours from mice which were infected with *T. congolense* and had been treated with " Bayer 205 " (0·0025 gm. and 0·005 gm. per 20 gm. mouse). A proportion of each set of subinoculated mice became infected up to 24 hours after treatment of the original mice. Somewhat similar results had been previously obtained by the author and Prieur with mice infected with *T. brucei*. In the case of mice inoculated from infected rabbits and cats infections were only obtained up to 1 or 2 hours after treatment.

With the object of going deeper into the matter careful observations were made regarding the incubation period and length of life in the 27 mice which became infected when inoculated from the *congolense* infected treated mice. The results obtained show that the probability of survival during the first 10 days is greater than in mice infected with

the normal untreated strain, but that the probability of mortality in the first 25 days is approximately the same in both groups.

The author next passed to an examination of the virulence of the relapse strain obtained from mice which had relapsed after treatment with " Bayer 205." All the subinoculated mice became infected, but the infections showed the same characters of diminished virulence.

W. Y.

Launoy (L.) & Ancelot (A.). Sur l'intérêt de la thérapie synergique étiologique (trypanocide). Nouvel exemple de son application.—[**Treatment with Combined Drugs (Synergy) in Trypanosomiasis.**]—*C.R. Soc. Biol.* 1933. Vol. 113. No. 24. pp. 871–873. [11 refs.]

Experiments are described indicating the advantages to be obtained from combining an antimonial preparation with " Bayer 205 " in the treatment of mice infected with *T. congolense.*

In the first series of experiments 25 infected mice were treated with a mixture consisting of 0·005 gm. of " Bayer 205 " and *70γ of Sb (antimony biopyrogallol-o-acetate of sodium). The blood of all of these animals was sterilized in 24 hours and only one relapsed. When the dose of the antimonial was decreased to 56γ, it was found that 12 of 15 mice were cured and three relapsed. A series of subinoculations were made after treatment to ascertain how long the heart blood remained infective. The subinoculations were always positive up to the 19th hour after treatment, but between this time and the 24th hour the results were irregular. When the doses of the drugs were increased slightly, analogous results were obtained, but rather more speedily. It is pointed out in conclusion that the antimonial preparation alone had but little action.

W. Y.

Dubois (A.). A propos de l'association Bayer 205 et émétique. [**Association of Bayer 205 and Tartar Emetic.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. June 30. Vol. 13. No. 2. pp. 143–147.

The author has studied the favourable results obtained by combining tartar emetic with Bayer 205 with the object of throwing light on the mechanism of the phenomenon. His technique was eventually the same as Pieraerts [see this *Bulletin, ante*, p. 115].

Rats infected with *T. tumba* were treated with moderate doses of Bayer 205 (1 cgm. per kilo) ; in certain cases the animals were cured and consequently the experiment failed ; but in the majority parasites were still present after 24 hours and rats were subinoculated, and then after some days at the time of relapse other passages were made and the first rat treated with tartar emetic. This should normally lead to the cure of the Bayerized rat in accordance with previous observations. In order to see whether the subinoculated rats had modified infections some were kept as controls and others treated with tartar emetic.

A number of experiments are given in detail from which it appears that the Bayerized rats themselves were sometimes cured by the subsequent dose of emetic, but the subinoculated rats were not cured by this drug. From this the author concludes that the activity of the Bayer-emetic association is a case of synergic medication, which cannot be

*γ = 0·001 mgm.

explained by a modification of the parasite. It is without doubt due to the presence of small quantities of Bayer in the circulation of the host which suffice to activate the tartar emetic. *W. Y.*

Pottier (R.) & van den Branden (F.). Note au sujet du tryparsamide ou tryponarsyl (glyphénarsine de la P.B. IV). [**Brands of Tryparsamide. Tests for Toxicity.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. June 30. Vol. 13. No. 2. pp. 187–197.

The authors point out that there are now on the market quite a number of brands of tryparsamide, and that these probably vary in purity and in toxicity. In the present work they have compared the toxicity of certain samples and describe what they regard as a standard technique for determining the toxicity of any sample of the drug.

It is noted that Launoy and Engler of the Rockefeller Institute give the lethal dose of tryparsamide for the rabbit as 0·9 gm. per kilo., and that they state that the dose which should be tolerated is 0·75 gm. per kilo., no more than 40 per cent. of the animals dying within a period of 7 days. When the observation was extended to 30 days Launoy and Engler found that doses of 0·85 gm. per kilo. gave 100 per cent. of mortalities, and doses of 0·75 gm. per kilo 50 per cent. of mortalities.

In previous work one of the authors had found that good samples of tryponarsyl (Meurice) and tryparsamide (Poulenc) were tolerated in doses of 0·75 gm. per kilo., and that all the rabbits survived for 7 days. It was therefore determined to ascertain the effects of larger doses. Four brands of the drug were tested ; the two above mentioned and also novatoxyl (Erich Boehden et Cie) and trypotan (Bayer). It was found that in each case the majority of animals survived a dose of 1·0 gm. per kilo. and that no difference could be discovered between the various brands.

In further experiments the dose was increased to 1·25 gm. per kilo. and all the animals survived the 7 days' observation ; no difference being seen between tryponarsyl, tryparsamide (Poulenc) and tryparsamide (Powers of Philadelphia). It was eventually found that the dose of tryponarsyl which gave 100 per cent. of deaths was 2·5 gm. per kilo. It thus appears that the tolerated dose and the lethal dose are much higher than those given by American and French authors. This fact is of importance in testing samples of drugs. For example, some time ago van den Branden examined a number of samples of tryparsamide which had been in the Congo for years ; some of them had become slightly yellow in colour. He found, however, that rabbits tolerated 0·75 gm. per kilo. of all the samples, and consequently concluded that they had undergone no increase in toxicity [*ante*, p. 116]. In light of his recent observations he re-examined two of these samples and found that although rabbits tolerated as before 0·75 gm. of the drug, doses of 1·25 gm. per kilo. killed almost 100 per cent. It is clear therefore that they had actually become more toxic during their prolonged sojourn in the Congo, because the fresh samples were easily tolerated in doses of 1·25 gm. per kilo.

The authors then pass to a consideration of the practical details of toxicity tests, and finally lay down the following rules :—

The test should be done on 5 rabbits of between 1,750 and 2,250 gm. in weight. The animals should be of the same race and free from all obvious blemishes ; males or non-pregnant females should be used. They should be kept under observation for 15 days before the test to

accustom the animals to the hutch ; they should be carefully looked after, well fed, and kept properly warm in cold weather.

The dose of drug given should be 1 gm. to 1·25 gm. per kilo. of weight ; it should be dissolved in 10 times its weight of distilled water, sterilized by boiling, and administered at 20° to 25°C. The solution should be injected slowly into the marginal vein of the ear. The animals should be kept under observation for 7 days, and during this time not more than 2 of the 5 should die ; the remainder should be in apparent good health. Samples intended for human use should pass this biological test. *W. Y.*

Barlovatz (A.). Sur certains accidents de cures au tryponarsyl. [**Accidents in Tryponarsyl Cures.**]—*Bull. Soc. Path. Exot.* 1933. June 14. Vol. 26. No. 6. pp. 850–856.

The author draws attention to certain grave accidents—sudden death and blindness—which he has encountered in the treatment of sleeping sickness by tryponarsyl during the year 1932.

The drug used was several years old ; the exact age is unknown, but it was certainly more than 2 years, which is the period for which the product is guaranteed. It was stored in a suitable place—dark, sufficiently ventilated and at a temperature usual for well-built houses in the tropics. All the injections were made in the author's presence ; he prepared the solutions (20 per cent.) himself, and the injections were made by native assistants. The usual dose was 2 gm. or less. In this paper the author confines himself to the grave accidents.

Deaths.—Certain solutions produced in the majority of patients rapid untoward results. In an hour or two the patients suffered from marked stiffness of the limbs, from pain in the kidneys, and sometimes from headaches ; often there are tremors and sometimes rigors and certain patients vomit. In slight cases these signs are transient, but in severe cases they may last for some days. Sometimes these symptoms do not subside and the patient dies in 24 to 72 hours, the fatal issue being often preceded by bloody vomit and motions. Of 1,700 patients treated with an average of 17 injections there were 22 rapid deaths undoubtedly due to the drug. Barlovatz then passes to a consideration of the technique as a possible cause of these catastrophes, *e.g.*, the purity of the water, sterilization of water and syringe and so forth, but he cannot explain the fatal results on any of these grounds. Nor are the hypotheses that death resulted from a toxaemia due to the sudden destruction of large numbers of trypanosomes, or that the patients were in a bad state at the time of treatment, any more satisfactory.

Blindness.—The author limits himself to a consideration of those patients who became suddenly blind. He encountered in 1932 eleven such cases and in only two was there slight improvement after some months. Brief details are given of each. In 8 the nervous changes were very slight at the time of treatment and the 3 who were not punctured could not be grouped as somnolent cases. In only one case were the doses at all large, whilst in three they were very small.

It is recorded as perhaps significant that of 45 patients treated on 26th October all became ill, 6 died, 3 became blind and 2 suddenly developed bad sight. The solution employed on this occasion certainly seemed very toxic. Certain bottles then contain a factor which produces blindness and which kills. It is noted that some of the bottles

contained fine powder, others large crystals, the volume of the same weight of the drug varying greatly. The normal white colour had in certain bottles changed to a yellow or rose colour, but such bottles were always rejected. Among the white specimens remaining there seemed to be no relation between the physical character and the toxicity. It is stated that death followed the injection of 1·4 gm. in a young patient who had previously tolerated several doses of 2·0 gm. ; all the patients injected with this particular solution suffered gravely. The drug, which looked perfectly good, came from a bottle which had been used with success two weeks previously ; apparently, therefore, the change had occurred after the opening of the bottle. The explanation cannot be that one consignment was bad, because only some samples of many consignments were poisonous.

Barlovatz concludes that tryponarsyl which has been stored in Africa for more than 3 years may become dangerous and produce death and blindness. He points out that this conclusion differs from that of VAN DEN BRANDEN [*ante*, p. 116], who tested the toxicity for rabbits of old samples which had been kept for a long time in the Congo and concluded that they had not deteriorated. [In a more recent paper summarized in this number VAN DEN BRANDEN has modified his previous views]. *W. Y.*

TANON, LASSABLIÈRE (P.) & PEYCELON (A.). Valeur comparée du sérum animal et de l'eau distillée comme excipient de la tryparsamide.—[**Comparative Value of Serum and Distilled Water as Excipient of Tryparsamide.**]—*Rev. Méd. et Hyg. Trop.* 1933. Mar.–Apr. Vol. 25. No. 2. pp. 83–85.

Experiments were undertaken to ascertain whether the results obtained in treating guineapigs infected with *T. gambiense* with tryparsamide were better when the drug was given in serum than when it was given in distilled water. The results suggested that there was no difference. *W. Y.*

TANON, LASSABLIÈRE (P.) & PEYCELON (A.). Contribution expérimentale à l'étude, la valeur comparée de la tryparsamide et la tséamine dans le maladie du sommeil. [**Comparative Value of Tryparsamide and Tséamine in Sleeping Sickness.**]—*Rev. Méd. et Hyg. Trop.* 1933. Mar.–Apr. Vol. 25. No. 2. pp. 81–82.

A few experiments were made on guineapigs infected with *T. gambiense* with the object of estimating the therapeutic value of " tséamine." The authors conclude from these experiments [which the reviewer regards as very unconvincing] that the action of tséamine is superior to that of tryparsamide. Further experiments show that the therapeutic action of tséamine is destroyed by heating. *W. Y.*

RODHAIN (J.), DUBOIS (A.) & HENDRIX (H.). Essais thérapeutiques de nouveaux composés antimoniaux dérivé de la quinoleine (Dn 9 à Dn 20 U.C.B.). [**Therapeutic Trials of New Antimonials derived from Quinoline.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Mar. 31. Vol. 13. No. 1. pp. 17–42.

This paper gives the results of testing certain new antimonial derivatives of quinoline, manufactured by the Union Chimique Belge, on laboratory animals infected with various strains of trypanosomes.

Four of the compounds, viz., Dn 9, Dn 12, Dn 17 and Dn 20, are pentavalent, and the remainder, Dn 7, Dn 8, Dn 11, Dn 14 and Dn 18, are trivalent. Various details regarding them, such as their chemical

constitution, their antimony content, and their toxicity for rats, are given in tabular form. Reference has already been made to Dn 7 and Dn 9 in a previous paper [this *Bulletin*, Vol. 29, p. 297] and the present work relates mainly to observations on the other compounds. They were tested mainly in rats infected with *T. congolense*, *T. evansi*, *T. brucei*, *T. tumba* and *T. rhodesiense*; and the results obtained are summarized in a series of tables.

It was found that all the compounds had a definite trypanocidal activity, but that the degree of activity varied according to the infection. Sterilization was only obtained with doses bordering on the toxic and *T. congolense* proved to be the most sensitive parasite. It was difficult to distinguish between the trivalent and pentavalent compounds in respect of their trypanocidal activity; in fact, the pentavalent compound Dn 20 proved just as rapid in its action as did the trivalent compound Dn 18. Apart from Dn 9 and Dn 18 all the compounds were so irritating that they could not be given subcutaneously. *W. Y.*

Fourneau (E.), Trefouël (J.), M. et Mme., Bovet (D.) & Koetschet (Pierre). Chimiothérapie des infections à *Trypanosoma congolense*. Action élective des composés organiques polyarsenicaux. [**Chemotherapy of** *T. congolense* **Infections.**]—*C. R. Acad. Sci.* 1933. Apr. 18. Vol. 196. No. 16. pp. 1173–1175.

It is well known that *T. congolense* infections have always exhibited a marked resistance to the action of the organic arsenical compounds. The authors have found, however, that this is not really a case of arsenic resistance, but that there are actually a whole series of arsenical compounds which are active in this infection. This property is possessed by very numerous organic arsinic acids characterized by the fact that their molecule contains at least two arsinic acid groups. Further details will be published later, and in this preliminary note the authors content themselves by giving a brief summary of the compounds and an indication of their activity on *T. congolense* infections.

W. Y.

Stein (L.). Ueber die Wirkung eines löslichen Wismutkomplexsalzes auf Trypanosomeninfektionen. [**On the Action of a Soluble Complex Bismuth Salt on Trypanosome Infections.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1933. Vol. 78. No. 5/6. pp. 489–496. [29 refs.]

Experiments were undertaken to test the value as a trypanocidal agent of a new soluble bismuth compound prepared by Rothmann of Berlin. The compound is the sodium salt of bismutho-dithiopyridin carbonic acid, the graphic formula of which is given: it is designated "R 141." It is a light yellow powder, readily soluble in water, gives an acid reaction with litmus and its bismuth content is about 40 per cent.

The drug was tested on mice infected with various strains (nagana, *T. equiperdum*, *T. equinum*, *T. rhodesiense*, *T. gambiense* and *T. congolense*). Although it had a favourable action it, as a rule, failed to cure; the best results were obtained by repeated small doses. It acted differently in the different infections and best with *T. congolense*.

W. Y.

NICOLLE (Pierre). Etude du pouvoir infectieux du sang et des organes de souris expérimentalement infectées par *Trypanosoma congolense* pendant la période de blanchiment qui suit l'injection de différentes doses de 205 Bayer-309 Fourneau. [**Infectivity of Blood and Organs of Mice infected with** *T. congolense* **after Injection of Varying Doses of Bayer 205.**]—*C. R. Soc. Biol.* 1933. May 5. Vol. 112. No. 16. pp. 1658–1660.

The object of the experiments described in this paper was to discover something about the distribution of the parasites responsible for the relapse in trypanosome infected mice treated with subcurative doses of " Bayer 205." Do the parasites completely disappear from the blood and take refuge in certain of the internal organs, and if so in which ?

It was found that when mice infected with *T. congolense* were given an intravenous injection of 0·002 gm. of " Bayer 205 " per 20 gm. of mouse, the parasites disappeared from the blood for 4 or 5 days, whilst, when the dose was increased to 0·004 gm., the time of disappearance was increased to 5 or 6 days. A series of experiments was performed in which infected mice were killed at various intervals after treatment, and their blood and emulsions of different organs—salivary glands, heart, lungs, kidneys, liver, spleen, ovaries, testicles and brain, were injected into healthy mice. The results of two such experiments are set forth in tables. From these tables it appears that after a dose of 0·002 gm. of the drug, although trypanosomes could not be detected by microscopic examination of the blood from the second to the fourth days, nevertheless subinoculation of the blood into fresh mice always produced infection. When the dose was increased to 0·004 gm. per 20 gm. mouse, microscopic examination of the blood was negative from the 23rd hour to the 5th day, and subinoculation of the blood into fresh mice failed to produce infection between the 31st hour and the 3rd day. Subinoculation of organ emulsions as a rule gave rise to infection, but sometimes failed to do so, especially about the time the blood was negative. The author is inclined to ascribe the infections following inoculation of organ emulsions as due to the small amount of blood they contained.

The question what happens to the parasite from the time the blood loses its capacity to infect fresh mice to the time of relapse is still left unsolved, but the author suggests that, as a practical measure in combined therapy, it would be as well to give the second drug some time (31 hours) after the " Bayer 205 " instead of giving both drugs about the same time. In other words that the second drug should be given at the period of maximum sterilizing effect of the " Bayer 205."

W. Y.

COLLIER (W. A.) & SEEGERT (J.). Die Bedeutung des Organismus für den chemotherapeutischen Heilungsvorgang. [**The Significance of the Host in Chemotherapeutic Cure.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. July. Vol. 37. No. 7. pp. 342–346. [19 refs.]

This paper lays stress on the importance of the host in chemotherapeutic processes. The author quotes extensively from the literature in support of his contention.

KOLLE showed that it was easier to cure rabbit syphilis at an early stage of the disease than later, and similar results were obtained by Collier and KRAUSE in trypanosomal infection of mice. Reference is

made to the fact that blocking of the reticulo-endothelial system inhibits the action of drugs. The same drug acts differently in different animals, *e.g.*, the chemotherapeutic index of atoxyl in nagana infected mice is $\frac{1}{2}$ to $\frac{1}{3}$ and that of neosalvarsan $\frac{1}{60}$; in human trypanosomiasis atoxyl was good, but neosalvarsan of little use. [Undoubtedly this statement expresses the general view, but whether it expresses a fact is, in the reviewer's opinion, a matter of doubt. Atoxyl has been extensively used in sleeping sickness and much is known about its action; the same cannot be said of neosalvarsan. To quote a single example, the results obtained by ZUPITZA (1920) in Togoland with neosalvarsan in 64 cases of sleeping sickness appear to have been dramatic (100 per cent. cured after an observation period of 11–19 months) [this *Bulletin*, Vol. 17, p. 328], and yet that observation seems to have attracted little or no attention. There are other examples of the abandonment of what seem to be most valuable drugs for little or no reason. Arsacetin in trypanosomiasis of laboratory animals is one of the most valuable of the aromatic arsenicals and yet it has never received a fair trial in man, probably because one of the few patients in whom it was used became blind. Yet atoxyl, which in laboratory animals seems to be a relatively very inferior drug, is extensively used, notwithstanding the fact that it has made countless patients blind. The reviewer merely calls attention to these facts in order to show how easily an "idée fixe" gets into the literature and remains there indefinitely, although it is based on little or no foundation of fact.] Quotations are made from PEARCE and BROWN and others showing that mice are cured by smaller doses of tryparsamide, antimosan, etc., than are rats and guineapigs.

The authors themselves, in their own experimental work, used three drugs, myosalvarsan, Fouadin, and Bayer 205, and they examined their actions on mice, guineapigs, and rabbits infected with the same strain of nagana. The mice were treated on the day after infection, and the guineapigs and rabbits on the 14th day of the infection. The drugs were always given subcutaneously. The results are summarized in the following tables :—

Myosalvarsan gm. per kilo.

	Dose tolerated	Dose curative.	Index.
Mouse	1·200	0·045	1/26·5
Guineapig	0·100	0·010	1/10
Rabbit	0·600	0·030	1/20

Fouadin gm. per kilo.

	Dose tolerated	Dose curative.	Index.
Mouse	0·500	0·150	1/3·3
Guineapig	0·210	0·140	1/1·5
Rabbit	0·080	>0·080	>1/1

Bayer 205 gm. per kilo.

	Dose tolerated	Dose curative.	Index.
Mouse	0·600	0·0014	1/428·5
Guineapig	0·200	0·007	1/42·8
Rabbit	0·600	0·006	1/100

From these results the authors conclude that, even with the same infection, each drug exhibits a different curative value in the different host, and that for each host it exhibits a different toxicity. *W. Y.*

ROSKIN (G.) & ROMANOWA (K.). Experimentell-zytologische Untersuchungen ueber die Einwirkung einiger chemotherapeutischer Stoffe auf Trypanosomen. [**Experimental Cytological Investigations on the Action of Certain Chemotherapeutic Substances on Trypanosomes.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. July 11. Vol. 129. No. 1/2. pp. 35–40. [17 refs.]

In this paper the authors describe a new technique for recognizing the early action of various drugs on trypanosomes both *in vivo* and *in vitro*.

The method is based on the investigations of UNNA, who prepared the leukobase of methylene blue, which is designated " Rongalitweiss." Roskin in a former paper had put forward the view that the staining of certain parts of cells (normal and pathological) by " Rongalitweiss " was due to the presence of a certain ferment in the protoplasm ; this is destroyed by heating to 80°C. and by long exposure to alcohol, formalin or X-rays, and is much damaged by KCN ; and when this has occurred the cell no longer stains with " Rongalitweiss." HIRSCH and BUCHMANN reached similar conclusions and called the ferment " Oxydoredukase." In normal trypanosomes the " Rongalitweiss " reaction is very pronounced, *i.e.*, portions of their protoplasm take on a distinct blue colouration, but this never extends over the whole cell body. In most of the trypansomes the portion of the body near the flagellum stains most intensely, and in the nucleus the karyosome stains more or less distinctly.

The authors' experiments were conducted as follows :—Dry blood films were made of the blood of a mouse heavily infected with *T. equiperdum*. A drug (stovarsol, tartar emetic, germanin, neosalvarsan, old salvarsan or trypaflavin) was then administered and more blood films made at intervals between 10 mins. and 48 hours later. All the films were then treated by " Rongalitweiss " as follows :—the freshly prepared material was poured on the films and allowed to act for 2 mins., the films were then rinsed in oxygen-free water and embedded in paraffin oil.

In the first experiment in which 0·4 cc. of a 1 per cent. solution of stovarsol was given to the infected mouse, it was found that in the blood films made 10 mins. later the trypanosomes no longer stained with " Rongalitweiss." Similarly, the trypanosomes in the preparations made after 20 mins., 30 mins., 60 mins., and 120 mins. all failed to stain. Details are given of the results obtained with the other drugs.

From this work the authors conclude :—

1. That by means of the " Rongalitweiss " method they have demonstrated a ferment-like factor in the nucleus and cytoplasm of trypanosomes.

2. With the assistance of this method they were able to detect an effect of various drugs on trypanosomes very early at a time when other methods failed to reveal any change in the nucleus or cytoplasm.

3. The action of the drugs examined was directed against the ferment-like factor (the Oxydoredukase).

4. Stovarsol and salvarsan exerted the most intense action.

5. In the case of germanin the disturbance in function of the Oxydoredukase is probably a secondary phenomenon.

6. The " Rongalitweiss " method permitted both *in vivo* and *in vitro* a differentiation in the character of the action of the various chemotherapeutic substances.

7. It also makes it possible to observe the relative changes produced by the various drugs in the nucleus and cytoplasm of the trypanosomes.

W. Y.

Halperin (E. P.). Zur Frage der Chemoflexion. [**On Chemoflexion.**] —*Zent. f. Bakt.* I. Abt. Orig. 1933. May 22. Vol. 128. No. 5/6. pp. 320–326. With 4 figs.

Halperin has reinvestigated the phenomenon of chemoflexion described in 1911 by Morgenroth and Rosenthal.

These authors injected mice of 15–20 gm. weight with trypanosomes (*T. brucei* Prowazek) ; when the peripheral blood contained between 50,000 and 300,000 trypanosomes per cc. the mice were treated with tartar emetic 0·2 cc. of a 1/1,000 solution subcutaneously. Within 70–180 minutes the parasites had disappeared completely from the blood. Counts were made every 10 minutes and the rate of disappearance of the parasites represented by a curve. Within a few days a relapse occurred, and when the number of parasites again reached between 50,000 and 300,000 per cc. a second dose of the same amount of tartar emetic was given and the rate of disappearance of the parasites again plotted on a chart. Morgenroth and Rosenthal found in most cases that the curve representing the rate of disappearance of the parasites of the first relapse was greatly prolonged and that the parasites had sometimes not completely disappeared after 24 hours. In no case did the authors succeed in transmitting this enhanced resistance to a new animal. To this phenomenon Morgenroth gave the name chemoflexion ; it was considered by him to represent the first stage of the development of drug-resistance.

In order the throw further light on the matter, Halperin has repeated and extended Morgenroth and Rosenthal's observations : in addition to *T. brucei* (Prowazek) he used *T. brucei* (Paris), *T. equiperdum* and *T. rhodesiense*. His technique was essentially the same as Morgenroth's. The phenomenon was obtained with all the strains, but only when small doses (0·2 cc. of 1/1,000 solution) of the drug were employed. In contrast to Morgenroth and Rosenthal chemoflexion was not, as a rule, seen by Halperin until the third or fourth relapse, but this varied considerably in the different animals. The increased resistance sometimes remained for several relapses and sometimes disappeared to reappear again. Subinoculation of the resistant parasites to a normal animal invariably caused the resistance to disappear. *W. Y.*

Lavier (G.). Sur le polymorphisme réel de certains trypanosomes réputés monomorphes. [**Polymorphism of Certain Trypanosomes considered Monomorphic.**]—*Ann. Parasit. Humaine et Comparée.* 1933. July 1. Vol. 11. No. 4. pp. 280–286. With 3 figs. [11 refs.]

The author has examined carefully a very old strain of *T. brucei* from Zululand, which has been maintained for more than 30 years by passage through mice at Mesnil's laboratory in Paris. Contrary to the generally accepted view, he found that this strain is not strictly monomorphic, since he encountered about 2 short forms without free flagellum among each 1,000 individuals examined. Prolonged passage through

small laboratory animals has therefore not entirely destroyed the polymorphic character of the strain, but has reduced it to a marked degree.

It is recorded that BRUCE (1911) had drawn attention to the fact that *T. evansi* was not strictly monomorphic, and that BLACKLOCK and the reviewer (1913) had noted the same of two strains of *T. equiperdum*. Lavier has confirmed these observations as the result of his examination of strains of *T. evansi* isolated respectively from a case of surra in Mauritius in 1925, and from a horse in Morocco in 1926, and also of a strain of *T. equiperdum* isolated in Algiers in 1922. Lavier is consequently of opinion that HOARE and COUTELEN's classification of the trypanosomes [see above] needs some slight modification. Section B should be grouped as follows :—

I. Polymorphic trypanosomes.

1. Forms without free flagellum, numerous ; transmitted cyclically by Glossina. *T. brucei* syn. *T. pecaudi, T. suis, T. equi, T. togolense, T. ugandae, T. somaliense* pro parte. *T. rhodesiense* and *T. gambiense* are considered as varieties adapted to man.

2. Forms without free flagellum, rare.

a. Transmission by direct contact.—*T. equiperdum*.

b. Transmission non-cyclical by various biting insects.—*T. evansi*.

W. Y.

YORKE (Warrington), MURGATROYD (Frederick) & HAWKING (Frank). **The Relation of Polymorphic Trypanosomes, developing in the Gut of Glossina, to the Peritrophic Membrane.**—*Ann. Trop. Med. & Parasit.* 1933. July 7. Vol. 27. No. 2. pp. 347–354. With 2 plates.

The authors confirm the work of TAYLOR [*ante*, p. 105] and his predecessors on the relation of the developing trypanosomes to the peritrophic membrane in Glossina.

These observations were made during experiments on the transmission of a tryparsamide-resistant strain of *T. brucei* through *G. morsitans* and *G. palpalis* [*ante*, p. 448]. In flies dissected 1–4 days after an infective feed trypanosomes could be found in the midgut multiplying in the lumen inside the peritrophic membrane and sections showed that a few forms were present in the space outside the membrane, reached apparently by passage round its free edge. After the first feed, however, on a clean animal they were no longer found inside the membrane but in great numbers outside it, eventually passing forward and reaching the proventriculus ; here they pass through the fluid secretion of the annular pad, from which the membrane is formed, and so reach the lumen of the proventriculus and oesophagus. Sections of the wall of the midgut, proventriculus and salivary gland of such a fly are reproduced and described. *A. G. B.*

KOFOID (Charles A.) & DONAT (Fae). **South American Trypanosomiasis of the Human Type—Occurrence in Mammals in the United States.**—*California & Western Med.* 1933. Apr. Vol. 38. No. 4. pp. 245–249. With 5 figs.

This paper, which contains nothing new, gives a general account of South American trypanosomiasis. The article, which was inspired by the fact that Kofoid has discovered *T. cruzi* in a cone nose bug (*Triatoma protracta*), which is known to occur throughout a large portion of California, was written in order that physicians attending patients bitten

by " kissing bugs " may be aware of the possibility of trypanosome infection and seek to differentiate between toxic results of the bite and an infection by trypanosomes. *W. Y.*

DE AZEVEDO (A. Penna). [In Portuguese and German.] Histologia pathologica da glandula thyreoide na fórma aguda da molestia de Chagas (Trypanosomose americana). Pathologische Histologie der Schildruese bei der akuten Form der Chagas-Krankheit (amerikanische Trypanosomiasis). [**Morbid Histology of the Thyroid Gland in Acute Chagas Disease.**]—*Mem. Inst. Oswaldo Cruz.* 1933. Vol. 27. No. 2. In Portuguese pp. 93–123. With 15 figs. on 14 plates. [44 refs.] In German pp. 124–138.

The author has made a study of the histological changes in the thyroid gland in 5 cases of acute Chagas disease in young children 4 to 20 months old. The subject is of importance, especially in view of the simultaneous occurrence of Chagas disease and endemic goitre in the same regions. A clinical account of each of the 5 cases is given, and this is followed by a detailed description of the histological appearances found in the thyroid gland in each patient.

All patients exhibited a diffuse hyperplasia of the thyroid, although the type varied from case to case. On the basis of Buerkle-de la Camp's classification the histological changes in the thyroid of each case can be described as follows :—Case 1♂, diffuse colloid microfollicular struma; Case 2♀, diffuse parenchymatous struma neonatorum; Case 3♀, intermediate form between 1 and 2; Cases 4♀ and 5♂ diffuse parenchymatous struma neonatorum. Thus, in three instances there was a typical picture of the diffuse parenchymatous goitre of the new-born, in one instance there was a diffuse microfollicular colloid goitre and in the other instance an intermediate form. All patients had shown trypanosomes in the blood, and leishmanial forms were found in the various organs, particularly in the heart muscle. In a single case parasites were even discovered in the epithelium of the thyroid. No inflammatory interstitial changes were seen in any of the cases. The author considers the diffuse parenchymatous goitre of the new-born to be the characteristic type seen in acute Chagas disease. The article is illustrated by 14 microphotographs. *W. Y.*

CHAGAS (Evandro). Novos estudos sobre a forma cardiaca da *Trypanosomiase americana.* [**Fresh Studies of the Cardiac Form of American Trypanosomiasis.**]—*Mem. Inst. Oswaldo Cruz.* 1932. Vol. 26. No. 3. pp. 329–338. With 7 coloured plates.

This article deals with the subject of cardiac arhythmia in Chagas's disease, to which reference has been repeatedly made in this *Bulletin* (Vol. 25, p. 789; Vol. 27, pp. 838 and 839 and Vol. 28, p. 377). Clinical details are given of four patients, and their electrocardiographic tracings.

In the first, a boy of 14 years, there was organic interference in auriculo-ventricular conduction with partial heart-block; in the second, a man of 22 years, there were signs of a diffuse myocarditis with resulting derangement of function evidenced by intraventricular blocking and myocardial irritability. The third, a man 26 years of age, suffered with deeper myocardial lesions affecting conductivity of the whole cardiac musculature—intra-auricular, auriculo-ventricular, intraventricular block and extrasystoles. Lastly, a man of 49 years,

showed signs of partial A V block, slight intraventricular and more definite intra-auricular block. The article, which is of greater interest to the cardiologist than the general practitioner, is illustrated by radiograms of the thorax and electrocardiograms depicting the conditions described in the text. *H. H. S.*

Campos (Ernesto de Souza) & Artigas (Paulo de Toledo). Alterações do pulmão na trypanosomiase americana experimental e contribuição para e estudo da natureza das cellulas phagocytarias do pulmão. [**Lung Changes in Experimental American Trypanosomiasis.**]—Reprinted from *Ann. Faculdade de Med. São Paulo.* 1932. Vol. 7. 23 pp. With 14 figs. (8 coloured) on 6 plates. [21 refs.] English summary.

A detailed study was made of the lungs of seven puppies infected with *T. cruzi* ; these animals acquired the infection congenitally from two mothers which had suffered from a chronic infection of the disease since 1927 and 1928.

In the blood vessels the adult flagellate form of the parasite was found lying free between the cells, and in the alveoli loose cells were seen, some of which were loaded with parasites. These loose cells were in every respect similar to the dust cells. In a few alveoli a parietal cell was found to be parasitized. Similar parasitized cells were found in the inter-alveoli tissue and, as the result of proliferation of these cells, the septa were thickened. The authors reach the conclusion that parasitism of the lungs by *T. cruzi* represents a systematic reaction of the phagocytic cells, and is essentially the result of a cellular defence mechanism against the invasion of the parasites.

W. Y.

Arantes (J. B.). Do comportamento do *Trypanosoma cruzi* no *Silenus rhesus*. [**Behaviour of** *T. cruzi* **in** *S. rhesus.*]—*Mem. Inst. Butantan.* 1931. Vol. 6. pp. 233–235. With 2 plates (1 coloured). English summary (9 lines).

This note draws attention to the fact that *T. cruzi* is very pathogenic for *Silenus* (*Macacus*) *rhesus*. Six of these monkeys, one of which was inoculated with the faeces of an infected *Triatoma infestans*, two with the blood of an infected guineapig, and three with the blood of an infected Silenus, all became infected and died of the disease.

W. Y.

Dias (Emmanuel). Immunité naturelle des animaux à sang froid vis-à-vis de l'infection par le *Trypanosoma cruzi*. [**Natural Immunity of Cold-Blooded Animals to** *T. cruzi* **Infection.**]—*C. R. Soc. Biol.* 1933. Apr. 27. Vol. 112. No. 14. pp. 1474–1475.

After briefly discussing previous literature dealing with this subject, the author decribes his own experiments which consisted in inoculating the blood of a guineapig infected with *T. cruzi* into reptiles (*Tropidurus torquatus* and *Ameiva surinamensis*) and batrachians (*Leptodactylus ocellatus*) ; and also the blood of an infected dog into *Bufo crucifer*. The result was always negative, and study of the peritoneal fluid of reptiles inoculated by this route showed that the parasites disappeared from lysis and phagocytosis in less than 4 hours.

W. Y.

Dias (Emmanuel). [In Portuguese & English.] Sobre um Schizotrypanum de um morcego do Brasil. (Nota preliminar.) [**On a Schizotrypanum from a Bat of Brazil.**]—*Mem. Inst. Oswaldo Cruz.* 1933. Vol. 27. No. 2. In Portuguese pp. 139–142. With 3 figs. on 2 plates. In English pp. 143–146.

The blood of a number of mammalia at Lassance (Minas Geraes) was examined for trypanosmes and 2 dogs, 4 armadillos and 5 bats were found to be infected. The parasite from the dogs and armadillos was identified as *T. cruzi* by means of inoculation and histological examinations.

Of 22 bats (*Phyllostomidae*) examined only 5 were found to be infected ; the abode of almost all of them was the ceiling of the house inhabited by the author. Morphologically, the parasites of the bat closely resembled *T. cruzi*, but subinoculation made into two guinea-pigs failed. Histological examinations were made of the tissues of three of the infected bats. In two of them no multiplication forms were found in the tissues, but in one (the blood of which was heavily infected) the author found in sections of the lung and small intestine two cells with numerous leishmaniform parasites.

The author believes that the parasite he has found in bats is a non-pathogenic parasite, possibly *T. vespertilionis*, and he remarks that the possible co-existence in bats of two trypanosomes so closely related as *T. cruzi* and *T. vespertilionis* must be borne in mind. *W. Y.*

Vaucel. Les acquisitions nouvelles dans l'étude des trypanosomiases. [**Recent Knowledge of Trypanosomiasis.**]—*Ann. de Méd. et de Pharm. Colon.* 1933. Jan.–Feb.–Mar. Vol. 31. No. 1. pp. 25–63.

This is a summary of recent work on trypanosomiasis. It contains nothing new (except the spelling of the reviewer's name, which passes through such forms as Burke, Yorbe, and Yorje). *W. Y.*

Ashley (J. N.), Browning (C. H.), Cohen (J. B.) & Gulbransen (R.). **The Antiseptic and Trypanocidal Properties of Some Anil and Styryl Derivatives of 4 Amino Quinaldine.**—*Proc. Roy. Soc.* Ser. B. 1933. Aug. 1. Vol. 113. No. B783. pp. 293–299.

Browning (C. H.), Cohen (J. B.), Cooper (K. E.), Ellingworth (S.) & Gulbransen (R.). **The Antiseptic and Trypanocidal Action of Some Benzoylamino Quinoline Anil and Styryl Compounds.**—*Ibid.* pp. 300–307.

These papers are of a chemical and technical nature and should be consulted in the original by those interested. *W. Y.*

Lloyd (Ll.). **Factors influencing Trypanosome Infection Rate in Tsetse Flies.** [Correspondence.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. May 5. Vol. 26. No. 6. pp. 555–556.

In this letter Lloyd continues the discussion between Duke and himself [*ante*, p. 453] on the subject of the influence of temperature on the infection rate of Glossina. No further notice seems necessary.

W. Y.

MISCELLANEOUS.

LAMBERT (Sylvester M.). **Some Polynesian Medical Superstitions encountered in the Cook Islands.**—*Jl. Trop. Med. & Hyg.* 1933. July 1. Vol. 36. No. 13. pp. 189–192.

In the Cook Islands, writes Dr. Lambert, one of the chief obstacles to dealing with the medical needs of the native population has been lack of knowledge on the part of the medical staff of the customs and medical lore of the people.

These natives, though they are the most intelligent and most modern of the South Sea Islanders, have a deep rooted belief in magic and witch doctors. The native beliefs retailed here chiefly concern leprosy and elephantiasis, diseases specially repugnant to a people of great physical perfection. These diseases are either the punishment of an avenging god for the breaking of a tabu or may be willed upon a member of the community by a sufferer. Instances are given. Lambert writes that it will be long before the Cook Islands native will believe that there is any relationship between elephantiasis and filariasis or that either is in any way connected with the bite of a mosquito. In one instance a father with elephantiasis willed the disease upon a worthless son ; in another upon a daughter who offended both by taunting her father with his deformity and " running around with the boys " ; in a third a man who was hated by the husbands for his conquests of their wives was made drunk, and the urine of a sufferer was mixed with his beer. Every time elephantiasis resulted.

There has been a small Medical Department in the Cook Islands for 40 years ; native medical practitioners trained at Suva are now to be established in each island of the group. *A. G. B.*

JACOCKS (W. P.). **Ceylon Health Units.**—*Indian Med. Gaz.* 1933. June. Vol. 68. No. 6. pp. 332–338.

A full account of the Ceylon Health Units, their organization and their work.

In the words of the author :—

" The object is to bring to rural areas the benefits of health protection which are now enjoyed by large towns and cities. This end is accomplished by dividing rural areas into suitable districts and introducing therein small but completely trained bodies of workers who remain permanently in the delimited area and undertake all public health problems. Their activities embrace health education, general sanitation, collection, tabulation and study of vital and morbidity statistics, control of preventable endemic and epidemic diseases, vaccination and preventive inoculation, maternity and infant welfare work, school health work, and adult hygiene."

Health unit work was commenced in Ceylon in 1926. In December 1932 eight units were in operation in an area of 856 square miles containing 440,000 people. A long extract is given from the 1921 Report of the Department of Medical and Sanitary Services [see Supplement, 1932, pp. 80–81] describing the activities of the unit. Medical officers of health, public health nurses, midwives and sanitary inspectors now attempt no field work till they have spent a period at specified tasks in the health unit organization. The first unit, Kalutara Totamune, is used by the department as a training station. In the selection of this first area essential points were that the leading people should earnestly

desire the work and that early co-operation of officials should be secured. The author writes :—

" It is probably unwise to attempt to interest villagers in serious health work in those sections where there is not a fair degree of prosperity. If a villager has to struggle for his daily bread, and to be content with scanty and mean clothes and primitive shelter, it is not reasonable to expect him to listen to health propaganda of any sort. After his poverty is somewhat reduced, his food and clothing reasonably assured, his fields productive and his house respectable, he will have time and inclination to consider other matters. Consequently remote or backward districts should first receive other fundamental attention."

Experience indicates that a population of about 80,000 can be successfully handled. A statement of expenditure is appended. [For details of this and the work done the paper must be consulted.]

A. G. B.

Southern Rhodesia. **Report on the Public Health for the Year 1932** [Askins (R. A.), Medical Director].—31 pp. 1933. Salisbury : Govt. Printer.

In his introductory remarks Dr. Askins says that the health of the colony can be stated to be definitely good and to compare well with that of other British territories ; special consideration has been given to the combating of malaria—the major health problem—the treatment of mental disease and to measures against leprosy among the native population.

Vital Statistics.—These concern the Europeans only ; no figures are given for natives, who numbered 1,055,000 (estimated) at the 1931 Census. The estimated European population was 51,150 ; the rate of natural increase was 13·3 per mille (15·26 in 1931). There were 1,166 births, a birth-rate of 22·8 (23·58) per mille, slightly lower than the Union of S. Africa. There were 485 deaths, or 9·48 (8·32) per mille ; here the rate is slightly higher than that of the Union.

A table gives the causes of European deaths in 1928–32 ; the first five entries are, in descending order, pneumonia and bronchitis, violence, cancer, heart diseases, malaria and blackwater ; tuberculosis comes eighth. There were 64 deaths of infants under 12 months, a rate of 55 (45) per mille, 8 per 1,000 below the previous 5-year average, and a lower rate than that of the Union or of England and Wales. The causes of death are analysed. A table shows that in the 10-year period, 1923–32, nearly half the deaths occurred in the first month, from causes operating before birth. Other causes are diarrhoea and malaria, pointing to the need for antenatal supervision of the mothers, more care of the babies' food and protection from malaria. Child Welfare societies do valuable work, but the M.O.H. of Salisbury regrets that his department has no control over the activities of health visitors.

There were 7 deaths of European mothers due to pregnancy and childbirth, a rate of 6 per 1,000 live births. Of the causes during the 5-year period puerperal sepsis was much the largest factor, followed by accidents of pregnancy and childbirth. The author emphasizes again the need for antenatal supervision, for the provision of hospital beds for confinements and for trained midwives ; the latter are essential in a colony where many mothers live long distances from medical help and female assistance in the home is often lacking. Fortunately S.

Rhodesia possesses a number of maternity homes provided with the aid of the Beit trustees. S. Rhodesia possesses excellent facilities for training general nurses but none for training midwives ; to obtain the necessary qualification it is necessary to leave the Colony, with the result that most of the midwives are untrained. During the year the Government made annual grants amounting to £1,762 towards the maintenance of maternity homes.

Infectious and Communicable Diseases.—A table shows those notified in 1932. It is headed, as regards Europeans, by chicken-pox, measles, whooping-cough, diphtheria.

Malaria.—There were 25 European deaths and 12 from blackwater, a total of 37 which is about the average of recent years. Malaria accounts for 8 per cent. of European deaths, including in 1932, 8 young babies ; " it constitutes what is perhaps the gravest health problem of the colony." Dr. Askins discusses this problem and suggests that the study of the mosquito-vectors may lead to its solution as it appears to have done in the Union. The Government has arranged for an expert medical entomologist to study the problem during 1933. He discusses also the chemotherapy of malaria. Government expenditure on quinine in 1932 was £2,152, and receipts from sales £1,835.

Leprosy.—The incidence of leprosy among natives has been found to be greater than was realized. About 1,000 cases were treated in 1932, mainly in two institutions. Grants have been given by the British Empire Leprosy Relief Association. The policy adopted is : voluntary measures as far as possible but the Leprosy Repression Laws are retained and compulsion is exercised when necessary.

Plague.—So far plague is unknown but it has reached the northern part of South-west Africa and crossed into Angola [see this *Bulletin*, *ante*, p. 565] and is therefore very likely to enter S. Rhodesia from the south. Careful watch is being kept for it both in rodents and man. A list is given of veld rodents which have been identified as carriers.

Helminthiasis.—Intestinal bilharziasis was found in 3·5 per cent. of 372 Europeans, and in 16·4 per cent. of 665 natives. Urinary bilharziasis was found in 8·8 per cent. of 781 Europeans and 30·9 per cent. of 893 natives. Hookworm infection was recognized in 14·3 of natives admitted to Salisbury Hospital during the year.

Other diseases mentioned are *yaws*, of wide occurrence in the lower part of the Colony ; *undulant fever*, two European cases ; *trypanosomiasis*, one case in a native from Portuguese East Africa ; 40 native cases of *smallpox*. *Pseudo-typhus* or tick typhus is becoming more common and can probably be contracted in any part of the country. No death has so far been recorded. *Venereal disease* cannot at present be effectively combated. Of *tuberculosis* among Europeans there were 17 deaths. Its incidence on the natives is unknown.

Of *diphtheria* 52 European cases were notified with 6 deaths among young children. Anatoxin is kept available at the Public Health Laboratory, Salisbury, and is issued at cost price. The parents were circularized about the known facts of immunization, the Press gave support, with the result that large numbers of babies and school children are now being immunized. Of *typhoid* there were 37 cases in Europeans, and of *cerebrospinal meningitis* 2 cases. Of *whooping cough* and *measles* there were 410 and 293 cases, with 17 and 3 deaths. " Whooping cough is a grave disease in S. Rhodesia." *Influenza* was epidemic and caused 17 European deaths. There were no cases of typhus fever or rabies.

General.—With reference to *mental diseases* a brief account is given of the Mental Treatment Act, 1930, and it is stated that a medical officer is to be appointed to the Ingutsheni Mental Hospital with first class experience of the treatment of the insane. As an outcome of the Conference convened by the League of Nations which met in Capetown [see this *Bulletin, ante*, p. 563] S. Rhodesia will adopt the Draft Convention for the *Sanitary Control of Aircraft.* Probably Salisbury Aerodrome will be declared a Sanitary Aerodrome and surveillance of passengers who have left an infected area within 6 days will be enforced. An area on the northern border of the Colony is being surveyed, in collaboration with the Health Division of the Rockefeller Foundation, to prove the absence of yellow fever.

Town planning is another subject discussed. Suburbs are springing up at the edge of the large towns without any co-ordination or regard for future development ; no land is being reserved. S. Rhodesia at present possesses no town planning legislation in the modern sense. A Bill has been prepared and is under discussion by various bodies to place in the hands of local authorities power of effecting town planning both within and without their borders.

A section on the health of the B.S.A. police is followed by one on the School Medical Service. A whole-time experienced doctor visits the girls' schools and schools in outlying areas while the rest are visited by Government Medical Officers. Each child undergoes four routine examinations in its school career. In 1932, 4,415 children were examined and the results are tabulated. The author draws attention to malnutrition which was evident in entrants and probably the result of the financial depression and to splenic enlargement noted in 62 children and practically all due to malaria. Bilharzia was noted in 25 [but it is not stated whether all were examined for the eggs of this parasite or only those who presented symptoms]. Generally, the health of the children was considered satisfactory. 1,640 underwent a dental examination. The Government Dentists, who have hitherto confined their attention to the school children, are now to look after the teeth of the police as well as do essential work for paupers and prisoners ; every member of the Police Force is to be examined once a year.

Under the heading, *Health of the Native*, it is stated that the greater portion of the native population is devoid of any means of medical treatment. A system of outlying dispensaries in charge of native orderlies under the supervision of European doctors is to be introduced and is already at work on a small scale with encouraging results. [It is not stated what training the native orderlies receive.] From the results of research into tuberculosis among natives applying for work at the S. African mines, where it is found that 72 per cent. have acquired infection before arrival, investigation is to be made on S. Rhodesian natives in two areas where government has established a scheme for treatment.

Native labour on mines and works.—The average number employed on mines was 36,068 ; there was a greatly diminished number of deaths from sickness, including a 22 per cent. drop in the mortality from pneumonia. An officer of the Native Department is attached to Dr. Askins' staff as Inspector of Compounds, with great advantage both to mine owners and employees. The Inspector sees that the minimum ration as laid down by law is issued, and sees to housing, latrine accommodation, prompt payment of wages, etc. A table of cases of sickness and deaths shows that after minor ailments and

accidents and influenza the chief cause of sickness was malaria, and the chief cause of death pneumonia. The death rate from disease per mille per annum has fallen from 17 and 18 in 1928 and 1929 to 9·5 in 1932.

Dr. W. K. BLACKIE reports on the Public Health Laboratory and Pasteur Institute, Salisbury, where 13,305 examinations were carried out. Among a number of details the following are of interest. 338 throat swabs were examined and cultured for the diphtheria bacillus and a positive cultural result was obtained in 55 instances. In 665 stool examinations (natives) *Schistosoma mansoni* was met with 102 times and *S. haematobium* 7 times; hookworm 95; *Ternidens deminutus* 12 [see this *Bulletin*, Vol. 29, pp. 69 and 403]. Of 170 positive bloods for malaria *P. falciparum* was found every time but two. It is noted that in assessing degrees of anaemia at 4,500 feet an average red count of 5,500,000 must be allowed for adult males and 5,200,000 for adult females. A transfusion service of 70 persons has been instituted and 31 blood transfusions, chiefly for blackwater, were carried out.

[This is a well arranged and clearly written report which will be read with equal interest by laymen and the profession. Subject to the financial bar Dr. Askins should have little difficulty in effecting the improvements he desires. Little seems to be known of the state of health of the million natives.] *A. G. B.*

LINDSAY (Kenneth). **Notes on Medical Practice on the Brasileno-Paraguayan Frontier.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. May 5. Vol. 26. No. 6. pp. 547–554.

The author draws on his own experience and, during a period of more than 30 years, that of his father, who, it is stated, has noticed the general health of the people slowly decline. He describes the land and its people, social conditions, the diseases met with and veterinary work. Rheumatic fever is said to have made its first appearance in 1929, and chorea about the same time. Leishmaniasis is described but without fresh information. Some practical hints are given of the treatment of the myiases. The contribution is of interest but not adapted to summary. *A. G. B.*

CULPIN (Millais). **An Examination of Tropical Neurasthenia.**—*Proc. Roy. Soc. Med.* 1933. May. Vol. 26. No. 7. pp. 911–917 (Sect. Trop. Dis. & Parasit. pp. 47–53). [17 refs.]

Originally when the term neurasthenia was popularized by BEARD in the eighteen sixties, it was regarded as a disturbance in the balance between nerve waste and nerve repair—a physical condition due to a physiological upset. From among the several conditions covered by the term FREUD thirty years later separated what he called anxiety neurosis and anxiety hysteria, better described as anxiety states, and RAYMOND and JANET the obsessional states. Anxiety and obsessional states together with hysteria are now considered upon a psychological basis and grouped as psychoneuroses. It is questionable whether any small group of cases still remains which might still be called neurasthenia, cases characterized by marked chronic physical and mental lassitude, and to be distinguished from another group which paraded under the guide of neurasthenia until distinguished by Farquhar BUZZARD as akin to manic depression and called by him autonomous depression. Minor psychoneuroses are very common

in this country—50 per cent. of a working population of 1,500 persons were found to be affected, but in no case was a diagnosis of neurasthenia made.

Turning now to the condition as it has been represented in tropical countries, some idea of the fundamental different conceptions of neurasthenia may be gained from the correspondence in the *British Medical Journal* in 1926. So called tropical neurasthenia may be very common in many warm countries but the author's own experience goes to show that a population may exist in a tropical country such as Northern Queensland without neurasthenia being anything but rarely seen. The causes of " tropical " neurasthenia are the same as those met with in temperate climes. Tropical neurasthenia affects those persons who would tend to break down wherever they were. The general picture of cases of neurasthenia seen in England from the tropics presents no difference from that seen in other groups—war neurasthenia, miners' nystagmus, telegraphists' cramp, traumatic neurasthenia. The tropical cases should be grouped as " minor psychoneuroses occurring in the tropics," and the term " tropical neurasthenia " should disappear.

These conditions are failures of adaptation dependent on predisposition. The stimulus needed to produce breakdown is in inverse proportion to predisposition and may consist in any of the difficulties or demands of life but never hard work. Some of the difficulties of emotional adjustment to harmful stimuli may be peculiar to the tropics, others are dependent rather upon the attitude to life than upon climate.

Prophylaxis lies in the psychological examination of the candidate for residence in the tropics. Such a method of examination may be learned and it will serve to detect all those with predisposition. This has been effectively demonstrated in the selection of candidates for the staff of the Anglo-Persian Oil Company. Not only is it essential that the medical officer making such selection should have the requisite knowledge but also the medical staff abroad should be trained to pay attention to matters psychological in dealing with sick persons.

H. S. Stannus.

CILENTO (R. W.). [**The Anne MacKenzie Oration : The Conquest of Climate.**—*Med. Jl. Australia.* 1933. Apr. 8. 20th Year. Vol. 1. No. 14. pp. 421–432.

An interesting and thought-provoking address delivered to a lay audience at Canberra. *A. G. B.*

MCMULLEN. Observations et expériences nouvelles sur le transport des moustiques par les aéroplanes. [**Fresh Experiments on the Transport of Mosquitoes by Aeroplanes.**]—*Bull. Office Internat. d'Hyg. Publique.* 1933. June. Vol. 25. No. 6. pp. 1024–1027.

In these experiments, marked *Aëdes aegypti* were released in passenger planes leaving San Salvador for Brownsville, Texas, and Cristobal (Canal Zone) for the same destination, and from Cristobal to Miami (Florida). In one series a total of 840 mosquitoes were released on 12 planes and about 8 per cent. reached the destination. In one instance 27 out of 80 did so, the voyage having lasted over 30 hours ; 26 of them were females and 20 were gorged with blood. Other similar data are given. In one case the mosquitoes were so importunate that the waiter was obliged to use an insecticidal spray. The author thinks

this was used in other instances also, for it was after a second warning had been given to desist from the use of the spray during the experiments that the biggest catch was made (21 out of 60). The longest persistence was over 79 hours, after ten landings, three of which were for the night. Mosquitoes of over 12 days of age, which had imbibed blood, survived the flights at least as well as those just emerged. It is believed that insecticidal sprays carefully carried out will completely clear aeroplanes of mosquitoes. *A. G. B.*

Toumanoff (C.). Sur un premier essai d'acclimatation au Tonkin de *Girardinus guppyi*. Remarques sur le facteur thermique de l'activité larvicide de ce poisson. [**Acclimatization of *G. guppyi* at Tonking.**]—*Bull. Soc. Path. Exot.* 1933. Apr. 5. Vol. 26. No. 4. pp. 632–638.

The author conveyed ten specimens of *Girardinus guppyi*, a viviparous S. American fish, from the Pasteur Institute, Paris, to Tonking. Two months later four females survived. From these in 18 months 708 fish were obtained in the laboratory and in the open air in 12 months 47 multiplied to 520. Trials of their voracity showed that this was four times as great at 27°–30° as at 16°–20°C., an observation which the author thinks has a practical bearing. It remains to be seen whether they would survive the attacks of larger carnivorous fish.

A. G. B.

Froes (Heitor P.). **Studies on Venomous Fishes of Tropical Countries. (On the Brazilian Species of the Genus *Thalassophryne*, Guenther.)** —*Jl. Trop. Med. & Hyg.* 1933. May 1. Vol. 36. No. 9. pp. 134–135. With 2 figs.

The author observes that the text-book accounts of vulnerant fishes of the genus *Thalassophryne* are incomplete or incorrect. There are six species, 4 of which are found in Brazil. Some experiments on a guineapig and a fowl are described, from which it is concluded that the action of the venom is general as well as local, acting on the nervous system. There was no haemolysis. *Thalassophryne punctata* is figured showing the two dorsal and one of the pectoral barbs. *A. G. B.*

Andrews (Mary N.). **The Incidence of Intestinal Parasites in the Wuhan Area.**—*Chinese Med. Jl.* 1933. Apr. Vol. 47. No. 4. pp. 390–396.

In October–December 1931 the Henry Lester Institute, Shanghai, maintained a laboratory in Hankow in connexion with hospitals for flood refugees. Patients from the refugee camps formed the material of this enquiry.

The routine followed was the examination of two fairly thick films of faeces in saline under a low power for detection of ova and for protozoa a thin emulsion in saline examined under the high power ; in certain cases an iodine film was also examined. The examinations concerned 632 patients and numbered 913 ; 508 or 80 per cent. showed parasites, 9·6 per cent. harbouring protozoa only, 54 per cent. helminths only, and 16 per cent. both types of parasite. The findings are tabulated, and compared with Faust and Wassell's survey of the adjoining city of Wuchang in 1921 [see this *Bulletin*, Vol. 19, p. 458].

Parasite	Hankow 1931	Wuchang 1921
Number of cases examined	632	359
Per cent. positive	80·3	76·8
	Cases	Per cent.	Per cent.
Entamoeba histolytica			
Free forms	34		
Cysts	63		
Total	97	15·0	2·5
Entamoeba coli			
Free forms	3		
Cysts	39		
Total	42	6·6	5·0
Giardia lamblia			
Free forms	2		
Cysts	16		
Total	18	2·8	3·0
Trichomonas hominis			
Total	61	9·4	0·6
Chilomastix mesnili			
Free forms	4		
Cysts	4		
Total	8	1·2	—
Balantidium coli	1	0·15	0·3
Endolimax nana			
Cysts	4	0·6	—
Iodamoeba butschlii			
Cysts	2	0·3	—
Tricercomonas			
Cysts	2	0·3	—
Ascaris ova	352	55·6	54·3
Hookworm ova	177	27·0	22·0
Trichuria ova	199	30·0	36·2
Trichostrongylus ova	3	0·4	—
Oxyuris ova	1	0·16	—
Strongyloides larva	3	0·4	0·3
Fasciolopsis buski ova	32	5·0	0·6
Clonorchis sinensis ova	50	8·0	—
Schistosoma japonicum ova	32	5·0	3·6
Taenia ova	1	0·15	—
Hymenolepis ova	1	0·15	—

The cases of *Fasciolopsis buski* infestation were traced to Hanchuan, a small town on the Han river, which would seem to be an unrecorded focus of infection. *Clonorchis sinensis* is not mentioned in the Wuchang report. It is acquired from eating raw fish, which the refugees are very likely to have done. Of the 32 cases of schistosome infection in only 5 did the stools contain blood and mucus and in three of these

there were also free forms of *E. histolytica*. The *E. histolytica* records are much larger in this than in the Wuchang series. The relation of intestinal flagellates to diarrhoea is discussed : there seems to have been little evidence of flagellate pathogenicity in these records.

A. G. B.

Veneroni (Carlo). Distribuzione dei parassiti intestinali nel basso-piano Yemenita. [**Intestinal Parasites in Yemen Lowlanders.**]—*Arch. Ital. Sci. Med. Colon.* 1933. July 1. Vol. 14. No. 7. pp. 398–400. English summary (5 lines).

Intestinal parasites are very common in the Yemen Lowlands. Positive findings were noted in 565 out of 700 specimens of faeces, 80 per cent. The protozoon most frequently encountered was *E. histolytica* in 102 (14·5 per cent.) and of helminthic infestations Ascaris in 120 (17 per cent.), *Sch. haematobium* [so stated in a table and said in the text to be the only species] in 65 (9·2 per cent.), *Taenia saginata* (5·5), *Ancylostoma duodenale* (3·7). Other parasites mentioned are Dracunculus in 10 per cent. and *W. bancrofti* and *F. hepatica* as " somewhat rare." The reasons given for the high incidence of these infestations are : The insanitary condition of the people, the scarcity of rain in general, but occasional flooding from the hills leaving small ponds in which men and animals bathe [this would hardly be a satisfactory explanation of the parasitism]. *H. H. S.*

Coulter (J. L. S.). **The Land-Leech in Ceylon.**—*Jl. Roy. Nav. Med. Serv.* 1933. Apr. Vol. 19. No. 2. pp. 105–108.

The Royal Naval Camp, Diyatalawa, Ceylon, is situated about 120 miles up country from Colombo at an altitude of 4,000 feet. On arrival here the ship's company of H.M.S. Enterprise was attacked by leeches (*Haemadipsa zeylanica*) with which in places the ground was thick. They progressed with astonishing speed. They covered the boots and penetrated everywhere including the boot eye-holes. The only efficient prophylaxis is tobacco. The presence of moistened tobacco in the region of the ankles prevents biting, and enables the wearer to walk with comfort where leeches abound. For removal of attached leeches the application of salt and water is advised. Some natives seem to be immune to leech bites when others are attacked.

A. G. B.

Sergent (Edm.). L'Institut Pasteur du Maroc à Casablanca. [**The Moroccan Pasteur Institute at Casablanca.**]—*Ann. Inst. Pasteur.* 1933. July. Vol. 51. No. 1. pp. 5–13. With 9 figs.

A history and description of the Pasteur Institute established at Casablanca, with photographs and plans. It began to function on January 1, 1932, with Dr. G. Blanc as Director. Like other Instituts Pasteur it is under the direction, scientific, technical and administrative, of the parent Institution at Paris. Nothing is said of the source of its funds. *A. G. B.*

STRACHAN (P. D.). **The Dressing of Granulating Wounds and Ulcers.**—*South African Med. Jl.* 1933. June 24. Vol. 7. No. 12. pp. 397–398.

The author writes, from the Botsabelo Leper Asylum—

" After removing all dead tissue and rendering the ulcer free from virulent pyogenic infection by the application of wet Dakin's solution compresses, or, in some cases, methyl violet, we cover the ulcer and a margin of healthy skin with a strip of elastoplast. This is left on for from two to four weeks. Any discharges that ooze through the plaster are wiped off, and the surface is dusted with boric acid powder, which forms a dry, odourless crust . . . the bandage should be applied, as directed, from the bases of the toes to above the site of the ulcer. . . . Under this treatment, we find that large ulcers of the legs, which could not be induced to heal under daily dressings, become covered with epithelialized scar tissue in a few weeks."

The advantages of the treatment were rapid healing and saving of time and dressing material. The author surmises that any durable undisturbed dressing would equal elastoplast and has begun to put this to the test. *A. G. B.*

ROBINSON (J. S.). **Treatment of the more Severe Cases of Simple Tropical Ulcer.**—*West African Med. Jl.* 1933. Apr. Vol. 6. No. 4. pp. 67–68.

A practical paper. The treatment of severe tropical ulcer is described, the scraping and cleansing under chloroform, the dressing, splinting, and grafting in full detail. The average stay of 62 cases was 28·4 days. *A. G. B.*

NORONHA (A. J.). **A Preliminary Note on the Prevalence of Rhinosporidiosis among Sand-Workers in Poona, with a Brief Description of Some Histological Features of the Rhinosporidial Polypus.**—*Jl. Trop. Med. & Hyg.* 1933. Apr. 15. Vol. 36. No. 8. pp. 115–120. With 13 figs.

The interest of this communication lies in its suggestion of a waterborne causation for rhinosporidiosis and its characterization as an industrial disease of occupation. Rhinosporidiosis, not at all a common disease, has been found to be so comparatively frequent among sand-workers in Poona as to make out a good case for association there of the occupation and the disease. The workers are divers who enter the river to collect sand, and the contention of the author is that the nasal mucosa is infected by contact with the water. Rhinosporidial polypi may occur not only in the nose and eye but also in the ear and as papillomata of uvula and penis. The polypus when removed is greyish white, has an appearance rather like coral and shows characteristic " shiny white spots representing the mature sporangium of the parasite." The histology of these polypi is now well-known since the publication of ASHWORTH'S monograph. *W. F. Harvey.*

HASLÉ (G.). Traitement des splénomégalies tropicales par la solution de citrate de Normet. [**Treatment of Tropical Splenomegaly by Normet's Citrate Solution.**]—*Bull. Soc. Path. Exot.* 1933. June 14. Vol. 26. No. 6. pp. 843–849. With 2 figs.

Since 1930 the author has treated 132 cases of splenomegaly at Hué, Annam, with Normet's citrate solution, with much success. The solution has now the formula :—

Citrate of soda	... ...	gm. 22·0
,, lime	... ...	,, 6·5
,, magnesia	... ...	,, 4·5
,, iron and ammonia	... ...	,, 1·0
,, manganese	... ...	,, 0·005
Distilled water Q.S.	... ...	cc. 1,000

The spleen in this disease may occupy the greater part of the abdomen or only pass the costal margin by a few centimetres. It is sometimes very hard, in other cases soft but resistant. It is usually moveable and may be prolapsed. An enlarged liver is found in 10 per cent. often accompanied by slight jaundice, sometimes by ascites and oedema of the legs. Anaemia is often extreme. The red cell count is about 3 millions, but may be as low as one million ; the haemoglobin figure averages 50.

The author thinks that this disease has close relations with malaria from which most of the patients have suffered. Splenic puncture practised in 55 cases has not shown parasites ; the author has found either plasmocytes with a rounded and excentric nucleus with basophil protoplasm, or polycaryocytes with 2 or 4 nuclei of the same structure as the plasmocytes. Normoblasts are found in the blood ; in only 7 patients have malarial parasites been detected there.

The citrate solution causes a striking change in the spleen both in its structure and volume. Normet and Tardieu believe that the plasmocytes, fixed cells, are transformed into polynuclears, mobile cells, ready to pass into the blood.

In the Annamite intravenous injections of the citrate are well tolerated in the daily dose of 15 cc. ; in the European there may be a violent reaction, which can be avoided by gradually increasing the dose. The author begins with two subcutaneous injections of 10 and 15 cc. on successive days, and from the 3rd to the 12th day part of the dose is subcutaneous and part intravenous. Three or four series of 12 injections may be given, at intervals of 10–15 days. Many details are given.

Of the patients treated 42 regained a normal spleen, 35 were much improved, 37 were improved, 18 were not benefited.

The author reckons that in 58 per cent. success was complete. The average duration of treatment was 4 months. In the two photographs the areas of the spleen before and after treatment are strikingly indicated. No relapses have so far been met with.

Brief notes are given of four cases. *A. G. B.*

i. Huard (P.). Remarques sur la pathogénie, les aspects cliniques et l'évolution des myosites et pseudomyosites exotiques à staphylocoques. [**Pathogeny, Clinical Aspects and Evolution of Myositis and Pseudo-Myositis due to Staphylococci.**]—*Bull. Soc. Path. Exot.* 1933. May 10. Vol. 26. No. 5. pp. 693–697.

ii. ——. Myosite et pseudo-myosite aiguës à staphylocoques chez le même sujet.—*Ibid.* pp. 698–702.

i. This account is based on 23 published observations. Discussing the relation between these affections and filariasis the author reaches the conclusion that such a relation has not yet been demonstrated. He distinguishes four forms of staphylococcal myositis, (1) very acute and rapidly fatal, (2) acute, (3) sub-acute. He includes apparently in this last group the suppurating muscular haematomas, very frequent

in the African negro, which contain chocolate pus or a red blood-like fluid. This form is not purely tropical, a case having been reported from France. (4) A myositis of "cold" evolution. BOUFFARD in discussion referred to cases in French West Africa in which a pasteurella was the infective agent [this *Bulletin*, Vol. 17, p. 242].

ii. The case of a Senegalese soldier landed at Marseilles is described with comments. Here there was a deep abscess in the left thigh, intermuscular, and another in the right quadriceps, strictly muscular; it is the former lesion to which the name pseudomyositis is given.

Diagnosis is made by blood culture, presence of glycaemia, and search for staphylococcus in the urine; a positive blood culture is of serious prognosis. For treatment insulin is useful when there is glycaemia; serum and vaccines are of not much value; the main treatment is surgical. [For recent literature of tropical myositis see this *Bulletin*, Vol. 28, pp. 46–49; 857]. *A. G. B.*

i. MILLER (Sinclair). **Protein Shock Therapy in Undulant Fever.**—*Lancet.* 1933. June 3. pp. 1177–1178.

ii. MANSON-BAHR (Philip). **Undulant Fever of the Abortus Type treated by Protein Shock.**—*Ibid.* pp. 1178–1179. With 1 chart.

i. In seven cases of undulant (abortus) fever T.A.B. treatment brought the disease to an end, in three with dramatic suddenness.

The author gives an account of the symptoms and course of the disease. He accepts a positive agglutination against *Br. abortus* of 1/80 or over as definite evidence of infection. His plan is to give a T.A.B. injection intravenously and to repeat it every 3 to 5 days. The summary of his cases shows that the disease had been in progress six months, 10 days, six weeks, more than 3 months, 3 weeks, 3 months and 2½ months, and that the titre of agglutination was 1/250, 1/5,000 (*melitensis*), 1/1,250, high, 1/320, 1/2,560, 1/1,250; in most instances there was agglutination to *melitensis* at a lower titre. There is no record of the isolation of *Br. abortus*.

ii. A very acute case of undulant fever of abortus type in which the organism was isolated from the blood and the fever was cut short abruptly after a month's duration by an injection of 50 million T.A.B. The serum reactions were investigated by Professor G. S. WILSON, who obtained a titre of 1/10,000 against *Br. abortus*. Recovery was uninterrupted. *A. G. B.*

BRUMMELKAMP (R.). Maagulcus en vegetatief zenuwstelsel bij den Javaan. [**Gastric Ulcer and the Vegetative Nervous System.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1933. June 20. Vol. 73. No. 13. pp. 770–796. With 4 graphs. [18 refs.]

A marked difference in the incidence of gastric ulcer is apparent between Javans (1 per cent.) and Chinese (10·1 per cent.). If then gastric ulcer develops on the basis of a disturbed sympathetic nervous system (BERGMANN), Javans should show a high degree of stability of this system. In addition KOUWENAAR holds that there is a shift of the orthosympathetic-parasympathetic equilibrium to the vagus side, that is to say a relative preponderance of parasympathetic activity. The author in his investigation of the sympathetic nervous system of the Javan has used the atropine test (DANIELOPOLU). The principle of the test is that organs innervated by the vegetative nervous system have a relative tonus which is the resultant of the vago- and sympathicotonus,

an example of which is afforded by the frequency of the heart beat. If the vagus component is eliminated by means of atropine, only the sympathetic component remains in action. Another line of investigation dealt with the secretory function of the stomach. This is governed by the vagus. By stimulation of the vagus a larger quantity of gastric juice is formed and its acidity is higher ; motility is excited ; emptying is quicker ; peristalsis is greater and more frequent and the tonus of the stomach wall is higher. Sympathetic action is in the opposite direction. In gastric ulcer gastric secretion is said to be more acid and motility greater than normal.

The author concludes from his tests in Javans that :—(1) Gastric ulcer is infrequent. (2) The atropine test shows no evident dominance of a definite vegetative tonus variation. (3) The gastric juice has a high acidity which may be indicative of a local hypertony of the vagus. (4) The emptying of the stomach is rather more rapid than normal, which is also an indication of local vagus hypertony. (5) No connexion between vegetative tonus and gastric ulcer could be definitely established. *W. F. Harvey.*

Aitken (A. Blair). **Remarks on Peptic Ulcer.**—*West African Med. Jl.* 1933. Apr. Vol. 6. No. 4. pp. 63–65.

The author records 48 cases of peptic ulcer at Lagos in natives of Nigeria, seen in a period of 15 months.

Peptic ulcer is usually regarded in Nigeria as a rarity ; in the author's cases the diagnosis was verified at operation : 4 were gastric, 44 duodenal ulcers ; 44 were in males. The symptoms had usually been present a matter of years. He notes the degree of induration often present and the frequency and extent of perigastric adhesions. Some degree of pyloric obstruction was common. The percentage of ulcers admitted to the Lagos hospital in 1932 was 0·9 [not 9 as in the table]. The diagnosis is discussed and the difficulties in a country where X-rays and fractional gastric analysis are seldom available. *A. G. B.*

Grillo (J.). Experimentelle Untersuchungen ueber Misch- und Sekundärinfektion. III. Mitteilung : Ueber den Verlauf einer Infektion mit Trypanosomen und Rekurrensspirochäten beim Meerschweinchen. [**The Course of Infection with Trypanosomes and Relapsing Fever Spirochaetes in Guineapigs.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. Apr. 28. Vol. 128. No. 3/4. pp. 252–265. [12 refs.]

The author concludes as follows :—

In guineapigs which are simultaneously infected with nagana and *S. hispanica* the trypanosomes are influenced in the same way as they are in mice : the incubation period of the nagana is lengthened, the flagellates frequently disappear completely from the circulation and the life of the animals is prolonged. It is observed that after the lengthened incubation period the trypanosomes do not correspond with those of the original strain but are relapse modifications ; this suggests that the changed course of the trypanosome infection depends on a nonspecific heightening of the specific immunity processes by the relapsing fever. Whereas in guineapigs desplenation, which damages the functioning of the reticulo-endothelium for some time, accelerates the trypanosome infection, after previous treatment with electrocolloidal copper which causes only a temporary injury to the R.E.S.,

the course of nagana is delayed as in animals with mixed infections. Since relapsing fever has a similar action on the R.E.S. it must be assumed that the delayed cause of the nagana is due in each case to the same mechanism, namely to over-regeneration of the functioning mesenchymal cells caused by the primary damage to the R.E.S.

A. G. B.

COCHRANE (E.) & BETTENCOURT-GOMES (S. C.). **Glandular Fever in the Tropics.**—*Lancet.* 1933. May 6. pp. 955–956.

HASSELMANN appears to have been the first to report glandular fever from the tropics [see this *Bulletin*, Vol. 29, p. 531].

Seven cases are here shortly described which occurred on the return of a football team from Trinidad to British Guiana. The onset was sudden and simultaneous. They suffered from fever and ten or more days later from enlargement of cervical and other glands, and debility lasting for some weeks. The patients were not seen in the febrile stage. One blood examination is recorded—White cells 8,400 ; polymorphs 31·5 per cent. ; lymphocytes 66 per cent. ; eosinophils 1 per cent. ; large mononuclears 1·5 per cent. Efforts to trace the source of the infection were fruitless.

A. G. B.

ELLIS (D.). [**The Incidence of Asthma in Port Sudan, with Special Reference to the Influence of Moulds.**]—*Guy's Hosp. Reports.* 1933. Vol. 83. No. 1. pp. 102–111. With 3 graphs. [Summarized in *Rev. Applied Mycology.* 1933. June. Vol. 12. Pt. 6. pp. 370–371.]

" Of the 50 cases of acute asthma investigated by the writer at Port Sudan, 43 developed the disease for the first time after coming to the town, indicating the existence of some asthmogenic factor in the locality. Climate was the first to be considered and it was ascertained that 44 of the patients suffered the most severe paroxysms in the winter. No correlation could be detected between the incidence of asthma and the factors of soil, vegetation, and dust.

" On a damp December day ten Petri dishes were filled with a medium of agar and 10 per cent. glucose, sterilized, and exposed to the atmosphere for nine hours, after which they were covered and five placed in the ice chest and five in the incubator. After three days well-developed colonies of *Aspergillus niger* and *Penicillium glaucum* were observed, 14 or 15 on each plate, those on ice being larger and growing more rapidly. When the experiments were repeated on a relatively dry, hot day in July, only one or two colonies were obtained among all the plates exposed.

" A concentrated emulsion, prepared from living spores of *P. glaucum* (which was found to give more definite reactions than *A. niger*) was injected through epidermal scratches into two of the patients, each of whom developed violent asthmatic and local symptoms within half an hour. In subsequent tests one minim of the standardized mould-containing fluid was injected intradermally on the outer side of the right arm, one minim of the saline solution used for dilution being simultaneously injected into the outer side of the left arm. Numerous control experiments were similarly conducted on normal persons as well as on those suffering from various pathological conditions, none of whom developed positive reactions. All but two of the asthmatic patients, on the other hand, experienced more or less pronounced

reactions. Attempts to isolate the fungus from the sputa gave negative results.

"Treatment by a process of desensitization has been instituted in Port Sudan, and so far the outcome has been very satisfactory, both with English people and natives. The injections have been started with single minim doses of the standard suspension and gradually increased to ten minims, the latter dose being applied weekly until the attacks cease. No adverse effects have followed the use of live cultures, and the efficacy of dead ones has not yet been determined."

DE LANGEN (C. D.). **Studies on Blood Diseases and Blood Regeneration in Java.**—*Proc. Roy. Soc. Med.* 1933. Apr. Vol. 26. No. 6. pp. 763–772 (Sect. of Trop. Dis. & Parasit. pp. 37–46).

De Langen has never encountered a case of pernicious anaemia in a native of Java, and the same is true for the anaemia of sprue, which it so closely resembles. Sprue is pre-eminently a disease of the Europeans, not of the 45 million native inhabitants, and this fact is borne out by Army statistics, which force consists of half Europeans and half natives. The racial incidence of the pernicious anaemia cannot, like that of sprue, be explained by the effect of climate; it certainly suggests some relation between these two forms of anaemia, especially as they both react to liver therapy, just as is the case with two other well known diseases, which do not occur amongst Javans, gastric ulcer and carcinoma of the stomach. The question of origin is difficult to determine; if these diseases are avitaminoses they must implicate a different class of substances from that already recognized. In laboratory experiments with diets, the author has succeeded in producing various anaemic conditions, but only by the intramuscular or intravenous injection of linolenic acid has he been able to produce an anaemia of the pernicious type.

The connexion between achylia gastrica and pernicious anaemia is emphasized, but a considerable proportion of ankylostomiasis patients also have achylia gastrica which is histamine-refractory.

Statistics show that pernicious anaemia occurs less frequently amongst people living in Southern countries, and the percentages of mortality in various countries, without discrimination of race, are as follows:—

North America	From 6·9–9·1
Norway and the Netherlands	,, 4·4–8·9
Italy	2·3
Ceylon and Japan	From 0·3–0·6
Java	None

Blackwater Fever seldom appears amongst the indigenous population of Batavia. It occurs frequently amongst the newcomers—the Europeans, Japanese and Chinese. The author has examined many cases in Java, but has never found a really clear instance of haemoglobinaemia; occasionally he has found bands of methaemoglobin, and this in his opinion indicates a grave prognosis. He has made numerous experiments to determine the concentration of the haemoglobin in the plasma before excretion in the urine takes place.

By the injection of small quantities of linolenic acid in rabbits, a definite haemoglobinaemia is produced, but only when this becomes very obvious is the kidney threshold passed and haemoglobinuria ensues. Possibly this point can be ascertained more simply by dietary experiments, as in rabbits fed on a diet rich in lecithin. He has been

forced to conclude that haemolysis in blackwater fever does not take place in the blood stream, but more probably in the kidneys.

Ankylostomiasis.—The causation of anaemia in this condition has been explained, either by the chronic loss of blood through the intestinal canal, or by the action of toxins secreted by the worms themselves. It is possible by chemical tests in this disease to demonstrate the presence of blood in the faeces in the majority of cases, and in trials on healthy persons, by the administration of blood *per os*, it is shown that not more than 2–3 cc. is necessary to give the reaction to the same intensity as that obtained in ankylostomiasis. This quantity is very small indeed compared with that physiologically destroyed. He therefore concludes that there is no increased haemolysis in this disease, but, on the contrary, the destruction of blood is less than normal and points to an aplastic condition, or injury of the bone marrow as the cause.

Blood regeneration.—In his investigations in Batavia on this subject, the author has used the Terwen method and has applied LICHTENSTEIN'S calculations. By this method the total quantity of urobilinogen excreted daily in the faeces is determined, and from this the corresponding quantity of haemoglobin is calculated. In Holland Lichtenstein found that the amount of urobilin excreted varies between 125 and 150 mgm. and according to these calculations the person consumes his own blood in 140 days. In ten healthy native males the author found an average excretion of 115 mgm. over a period of ten days, which corresponds to a maximum life span of the corpuscle of 174 days, and in 5 severe cases of ankylostomiasis, the excretion was even less, so that in this disease there appears to be a much slower rate of blood destruction than normal. As the result of various investigations, he believes that diet exercises a great influence on the rate of blood destruction and regeneration.

Resisting Power of Corpuscles.—The haemolytic power of the lipoid layer of the corpuscles can be expressed in the quotient $\frac{\text{cholesterin.}}{\text{lecithin.}}$ It is considered that this co-efficient is governed by diet. In fasting animals and in rabbits fed only on grass and turnips, the resistance increases, but regeneration decreases at the same time. The author found that if a grass-fed rabbit was bled, it took a long time before the blood condition again became normal ; but if the animal be fed on oats, a large number of reticulocytes appeared, and the number of red cells is restored in half the time taken by the grass-fed animal, while the addition of lecithin to a turnip or grass diet, has the same effect as that of pure oats.

From the observations on the lecithin and cholesterin content, it appears that in the process of blood destruction and regeneration, it is not the concentration of the different lipoid and fat fractions that is the important factor, but their mutual relations, and this balance depends upon the nature of the diet.

The Impulse to Blood Regeneration.—The impulse to blood regeneration by the marrow can be effected by products set free from destroyed erythrocytes in conformity with MIYAGAWA'S theory of auto-regeneration. The author has found that the injection of whole blood provokes a good reaction, but not so great as that following the use of haemolysed corpuscles, and that bilirubin exerts a haemopoietic action on anaemic animals, but less than that produced by haemolysed red cells. The injection of splenic tissue has a different effect. Here recovery

from anaemia is slower than usual, but the number of reticulocytes is increased in proportion to the degree of anemia, thus indicating stimulus of the marrow ; but here again the effects of diet must be taken into consideration. *P. H. Manson-Bahr.*

Azmy (Soliman), Effat (Sayed) & Neshoukati (H.). **An Investigation of Anaemias in Egypt. Analysis of Fifty Consecutive Cases.**—*Jl. Egyptian Med. Assoc.* 1933. Apr. Vol. 16. No. 4. pp. 258–267.

Of the 50 consecutive cases of anaemia 4 were associated with chronic gastritis, 20 with ankylostome infection and 25 with chronic dysentery, chiefly bilharzial with or without ankylostomiasis.

In the dysenteric series the factors responsible for the production of anaemia were (1) loss of blood in the stools—a minor factor : (2) ankylostoma infection : (3) deficient absorption of iron due to the associated gastro-enteritis. When large doses of iron are given to make up for this, especially when dilute HCl is given as well, sufficient iron is absorbed and the anaemia improves. The improvement in the blood picture was strikingly independent of the improvement in the local dysenteric condition.

In the ankylostome series the probable factors in the production of the anaemia were (1) blood loss from the bowels—a very important one [see Wells, this *Bulletin*, Vol. 29, p. 421, where 0·84 cc. is the daily loss to be debited to each worm] : (2) a " toxic anhaemopoietic " factor put in evidence by a low reticulocyte count.

The authors give details of their five cases of chronic gastritis anaemia and note that " recent work is tending to reduce all primary anaemias to terms of failure of gastric function." The treatment of the 50 cases that gave the best results was inorganic iron by mouth in the form of ferrous sulphate exsicc. 0·30 gm. t.d.s. or reduced iron 2 gm. t.d.s. with dilute HCl in cases of achlorhydria. *A. G. B.*

Negroni (P.) La déviation du complément dans les affections cutanéo-muqueuses à Monilia. [**Complement Deviation in Muco-Cutaneous Affections due to Monilia.**]—*C. R. Soc. Biol.* 1933. Vol. 113. No. 21. pp. 476–478.

The author demonstrated that inoculations of *Monilia albicans* may produce intertrigo, vaginitis and onychia, and that antibody is constantly present in the serum of such subjects after a period of 20 days. Formol-saline extracts of monilia cultures were used as antigen, the technique being similar to that of the Wassermann reaction. Nineteen cases of cutaneous moniliasis were studied ; 13 were strongly positive (+++), 3 were weakly positive (+) and 3 yielded doubtful types of reaction. When the duration of the lesion exceeded 20 days positive results were obtained in 84 per cent. of cases. *N. Hamilton Fairley.*

Walch (E. W.) & de Moor (C. E.). In den Tropen erhaltene Resultate der Untersuchung von Fäzes und Harn auf Typhusbakterien mit Einschaltung der Mullerschen oder Kauffmannschen Nährböden. [**Effect of Interpolation of Muller or Kauffmann's Media in the Examination of Faeces and Urine for Typhoid Organisms.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. June 12. Vol. 128. No. 7/8. pp. 530–536. With 1 fig.

This investigation was concerned with the possibility of improving results by inoculation of faeces and urine in Muller's medium (sod.

tetrathionate) or in Kauffmann's medium (sod. tetrathionate with 1–100,000 brilliant green) before planting out on chloral-Endo plates. Addition of 1–1,000 chloral to an Endo plate prevented overgrowth by proteus bacilli while typhoid organisms were not affected. Dysentery organisms, however, were inhibited in their growth. Neither the Muller nor the Kauffmann method was successful for the isolation of dysentery organisms. No satisfactory enrichment medium for Paratyphoid A bacteria exists. Both the above enrichment methods are better than direct plating for paratyphoid food poisoning organisms. Muller's method was inferior to the direct method in the case of typhoid bacteria, while the Kauffmann method in combination with the chloral hydrate Endo plate gave as good, but no better results.

W. F. Harvey.

David (J. Christodoss) & Vareed (C.). **The Action of Quinamine on the Heart.**—*Indian Jl. Med. Res.* 1933. Apr. Vol. 20. No. 4. pp. 1005–1008. With 2 graphs.

Chopra and David (1927) published the first account of the pharmocological action of quinamine, an alkaloid of cinchona bark, isolated by Hesse. The work here described was undertaken to ascertain whether the drug would be useful in the treatment of auricular fibrillation. In dogs and cats it was found to cause a fall of blood pressure, and in small doses an apparent stimulation of the auricle ; no favourable effect on experimentally induced auricular fibrillation. *A. G. B.*

Lal (S.). **A Preliminary Report on the Active Principle of Bael.**—*Jl. Indian Med. Assoc.* 1933. June. Vol. 2. No. 10. pp. 391–395. With 11 graphs.

Bael fruit pulp yields a substance Marmelosin, pharmacologically very weak, for very large doses are required to produce any action on any organ. It acts directly on the muscular tissue. The actions of Liq. Ext. of Bael and of Marmelosin are similar. Inhibitory action of Marmelosin on peristaltic movements of gut can help to check those cases of diarrhoea due to excessive stimulation of motor activity. Tone increase is too slight to be of any consideration. But the facts that the amount of Marmelosin in Bael is little, and that very high doses of it are necessary to produce an action in experimental animals, lead to the conclusion that it plays little or no part in Bael therapeusis. At this stage it can only be said that action of Bael in diarrhoea and dysentery must be due to the quantity of mucilage and tannin present in it. *H. M. Hanschell.*

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HASSELMANN-KAHLERT (Marg.). Meine "superkalorische" Säuglingsnahrung mit besonderer Berücksichtigung des Energiequotienten beim Säugling in den Tropen.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Sept. Vol. 37. No. 9. pp. 399–408. With 3 figs.

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KHOURI (J.). Caractères morphologiques et biochimiques d'une *Monilia* isolée des crachats d'un malade atteint de blastomycose pulmonaire.—*Bull. Soc. Path. Exot.* 1933. Jan. 11. Vol. 26. No. 1. pp. 7–9.

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TILLEMA (S.). Pyomyositis tropica.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1933. June 6. Vol. 73. No. 12. pp. 760–761.

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REVIEWS AND NOTICES.

STANNUS (Hugh Stannus) [M.D., Ph.D. (Lond.), F.R.C.P. (Lond.), M.R.C.S. (Eng.), D.T.M. & H. (Cantab.), etc.]. **A Sixth Venereal Disease. Climatic Bubo. Lymphogranuloma Inguinale. Esthiomène. Chronic Ulcer and Elephantiasis of the Genito-Ano-Rectal Region. Inflammatory Stricture of the Rectum.**—pp. xii+270. With 9 plates. 1933. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, Covent Garden, W.C.2. [12s. 6d.]. [Review appears also in *Bulletin of Hygiene*.]

The identity of climatic bubo with lymphogranuloma inguinale has now been established, as also the fact that the disease is conveyed by venereal infection. This justifies the author's main title, "A sixth venereal disease," the other five V.D.'s being, syphilis, gonorrhoea, chancroid, the genital infection of Vincent's organism, sometimes called "the Fourth Venereal Disease" and Granuloma Venereum, or Ulcerating Granuloma of the Pudenda. The present work is an exhaustive critical review of the literature on the conditions mentioned; it will be found very valuable as a work of reference and particularly so by English and American readers since most of the articles reviewed are in other languages. (In the first 435 of the author's 933 references, which date from the year 1786, only 44 of the articles had appeared in English or American journals or books.)

The more important articles have appeared in the last five or six years and have been summarized by the author in this *Bulletin*. So far, however, the subject has been by no means clearly dealt with in text books on V.D. At the same time, it is highly important that workers in V.D. Treatment Centres should be well acquainted with it because the disease appears to be increasing on the Continent, and there is a strong possibility of its doing so in this country. In such an event the danger of its being overlooked, or confused with bubo resulting from chancroid, is likely to be prevented by a study of this book.

After historical reviews of lymphogranuloma inguinale and climatic bubo and establishment of the identity of the one with the other, the geographical distribution, clinical manifestations, aetiology, pathological changes, diagnosis and treatment are dealt with fully, including the important skin tests introduced by FREI. The work also includes a review of the literature on experimental transmission to lower animals and then presents the weighty evidence supporting the close aetiological relationship of lymphogranuloma inguinale to the conditions known as esthiomène, elephantiasis of the genito-ano-rectal region and inflammatory stricture of the rectum.

In a special chapter the author discusses the nomenclature, which is at present unsatisfactory. He favours the term "poradenitis" for climatic bubo and lymphogranuloma inguinale, while for certain sequelae one might use such terms as "poradenitic elephantiasis" "poradenitic stricture of the rectum" and (for esthiomène) "the poradenitic genito-ano-rectal syndrome."

The author has performed a valuable service in compiling this book, which must have entailed an immense amount of labour. It clarifies a subject that must, hitherto, have appeared very confusing to many of those who are likely to encounter the disease in their clinical work.

L. W. Harrison.

MCAUSLAND (Stuart) [B.A.(Lond.), M.D., Ch.B.(Liv.), M.R.C.S.(Eng.), L.R.C.P.(Lond.), etc.]. **The Cure of Haemorrhoids, Varicose Veins and Ulceration, and Allied Conditions: by Modern Methods of Injection and Bandaging.**—pp. vi+63. With 11 illustrations. 1933. London: John Bale, Sons & Danielsson, Ltd. [3s. 6d.].

The author in a foreword states that this book is based upon a "haemorrhoid" experience of eleven years and over 1,000 cases; and a

" varicose vein " experience of seven years and over 3,000 cases. He advocates the now well known 'injections'—quinine urethane mixture for varicose veins by the empty vein technique ; and carbolic acid in almond oil for internal haemorrhoids. His respective injection techniques are carefully described and the book must be of undoubted value to any practitioner who wishes to undertake these treatments. Those already experienced will perhaps envy the author his enthusiasm after so large an experience, but nevertheless remain of opinion that the enthusiasm is too uncritical. *H. M. Hanschell.*

GHOSH (Birendra Nath) [F.R.F.P. & S. (Glas.), etc.]. **A Treatise on Materia Medica and Therapeutics including Pharmacy, Dispensing, Pharmacology and Administration of Drugs.** 13th Edition.—pp. xv+712. With 3 figs. 1933. Calcutta : Hilton & Co.; and London : H. K. Lewis & Co., Ltd. [Rs. 7/8—or 12s. 6d.]

A book which is in its thirteenth edition does not call for a detailed review. Clearly it has met a need. It is not therefore necessary to do more than indicate its contents. The work is divided into seven parts—Materia Medica Proper (pp. 1–47) ; Pharmacy and Dispensing (pp. 48–73) ; Administration of Drugs (pp. 74–90) ; Pharmacology and Therapeutics (pp. 91–628) ; Vaccine and Serum Therapeutics (pp. 629–654) ; and Organotherapy, Radiation Therapy and Indian Indigenous Drugs (pp. 659–712). The preface speaks of drastic revision necessitated by the publication of the British Pharmacopoeia, 1932, and that the work is up to date is shown by the inclusion of atebrin and other drugs of recent introduction in tropical medicine. The work would appear to be a useful source of reference on the subjects with which it deals. *A. G. B.*

KIKUTH (Walter). **Die Bartonellen und verwandte Parasiten bei Mensch und Tieren.** [The Bartonellas and Related Parasites in Man and Animals.]—Reprinted from *Ergebnisse d. Hyg. Bakt. Immunitätsforschung u. Experim. Therap.* 1932. Vol. 13. pp. 559–619. With 12 text figs. [10 pages of refs.]

In the review of KIKUTH'S article on Bartonellas and allied organisms (this *Bulletin,* Vol. 30, p. 572) the discovery of Bartonella in the blood of splenectomized rats is erroneously attributed by the reviewer to LAUDA. This observer, as the article points out, noted the anaemia which developed in these animals after splenectomy but failed entirely to discover any organism to account for it. He concluded that an ultramicroscopic virus would prove responsible. On learning of LAUDA'S work Martin MAYER suspected that the cause of the anaemia was probably *Bartonella muris* which he had described in 1921. He quickly demonstrated the appearance of the parasite in the blood of rats subjected to splenectomy, a fact overlooked by LAUDA, and proved that it was actually the cause of the anaemia as he had suspected. *C. M. Wenyon.*

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